HUMAN MILK FORTIFIER AND MEDIUM CHAIN TRIGLYCERIDE OIL FOR WEIGHT GAIN IN VERY LOW BIRTH WEIGHT NEONATES: A RANDOMIZED CONTROLLED TRIAL

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Dedicated

to

my Family

&

Teachers

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Dr. Navotam

LIST OF ABBREVIATIONS

AGA	-	Appropriate for gestation age
BPD	-	Broncho pulmonary dysplasia
BW	-	Birth weight
CLD	-	Chronic lung diseases
EBM	-	Expressed breast milk
EUGR	-	Extrauterine growth restriction
GIT	-	Gastrointestinal tract
HMF	-	Human milk fortifier
IUGR	-	Intrauterine growth restriction
IVH	-	Intraventricular hemorrhage
LBW	-	Low birth weight
LOS	-	Late onset sepsis
LSCS	-	Lower Segment Cesarian Section
MCT OIL	-	Medium chain triglyceride oil
MEF	-	Minimal enteral feeding
NEC	-	Necrotizing enterocolitis
NICU	-	Neonatal intensive care unit
NPO	-	Nil per oral/ Nothing by mouth
NVD	-	Normal vaginal Delivery
OPD	-	Out Patient Department
PDA	-	Patent ductus arteriosus
PMA	-	Post menstrual age
ROP	-	Retinopathy of prematurity
SGA	-	Small for gestational age
US	-	Ultrasonography
VLBW	-	Very low birth weight
WHO	-	World Health Organization

ABSTRACT

BACKGROUND: Poor weight gain and postnatal growth of very low birth weight neonates continues to be a major problem as they are born with limited nutrient stores and have higher nutritional demands which are not met by breast milk. Hence require fortification with HMF/ MCT oil are being used for additional benefit.

OBJECTIVE: Main aim is to compare the weight gain pattern in VLBW neonates supplemented with HMF v/s HMF + MCT oil to expressed breast milk. Secondary outcome to compare the duration of hospital stay, Incidence of BPD, ROP, sepsis, IVH and NEC.

Material and Methods: Non blinded, Randomized Control Trial involving preterm neonates weighing < 1,500 g at birth, admitted to a neonatal intensive care unit. 90 subjects were randomized into two groups (45 neonates in each group): Group A: EBM+HMF, Group B: EBM+HMF+MCT oil. Fortifiers were added to expressed human milk when feeding volume reached 100 mL/kg/day.

Results: Randomized control trial performed on 90 neonates, 45 neonates in each group**.** These groups were comparable in term of weight and duration of hospital stay. The mean weight gain during and after follow up in group A and group B was 1831.33 ± 1934.94 gm and 1900.22 ± 1239.61gm and 2693.22 ± 510.54 gm and 2858.11± 407.09 gm respectively and the mean duration of hospital stay was 33.84 ± 15.84 days and 33.62 ±18.33 days in EBM+HMF and EBM+HMF+MCT oil group respectively. The difference was not statistically significant.

Conclusion: Comparing these two groups, we observed that fortification of human milk with HMF or HMF+MCT don't show any significant increase in weight gain and decrease in hospital stay.

Keywords: HMF, MCT OIL, neonates, weight gain

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INTRODUCTION

Very low birth weight (VLBW) neonates remain a significant health problem in the world as they are closely associated with neonatal mortality and morbidity. WHO defines very low birth weight neonates as birth weight less than 1500 regardless of gestational age.[1] They comprise 4-7% of the total live births and account for 30 – 40 % of total neonatal deaths.[2] Most of these deaths can be prevented by providing extra attention to warmth, prevention of infections and more importantly with optimal nutrition.[3]

VLBW is a result of preterm labor or intrauterine growth retardation or both. IUGR is multifactorial and is due to maternal, placental, fetal disorders. In developing countries, major reason of VLBW is lack of maternal nutrition (maternal undernutrition) and preterm deliveries. Intrauterine growth retardation is an additional risk factor in the growth of preterm neonates.[4] Most of VLBW neonates are usually born before 32 weeks gestation and since intrauterine accretion of nutrients occurs mainly in the later part of the third trimester, they have low body stores and are born with limited nutrient reserves.[5] Hence, aggressive nutritional management during first week of life influences immediate survival and subsequent growth and development of VLBW neonates.[6] Moreover, medical conditions associated with prematurity also alter these neonates' requirements thus further complicating the delivery of nutrients to them.[5] VLBW neonates at risk of developing short- and long-term morbidities such as hypothermia, hypoglycemia, increased risk of sepsis and feeding difficulties.[7] They are at additional risk because of immaturity of multiple organ systems, including risk of development of intracranial hemorrhage, respiratory distress, sepsis, risk of development of ROP, and gastrointestinal disorders (NEC), risk of chronic lung disease [(also known as Bronchopulmonary dysplasia (BPD).[4]

Poor weight gain and postnatal growth of preterm neonates continues to be a major problem.[5] Extra uterine growth restriction (EUGR) is a

major problem in VLBW neonates. It is defined as having a growth value of <10th percentile of intrauterine growth expectation based on postconceptional age at the time of discharge to home.[8]

EUGR is descriptive of static growth resulting from early weeks of life and suggests that it not only affects their weight but also length and head circumference.[8] Growth failure in VLBW neonates' results from the complex interaction of many factors like genetic and environmental factors, inadequate nutrition, morbidities affecting nutrient requirements, endocrine abnormalities and treatments [9]; It has been seen that low intake of protein and energy during the first week of life is responsible for impaired neurocognitive development.[10] Inadequacy of nutrition is related to decreased number of brain cells as well as deficits in behavior, learning and memory.[8] To overcome these problems, it is important to initiate nutrition at earliest.

Human milk is considered as the best and the first choice for enteral feeding for the neonates because of its several nutritional and immunological advantages. Bioactive molecules in human milk are important components of the innate immune system.[11] Though expressed human milk is the first choice for feeding for VLBW neonates, it has inadequate amounts of protein, energy, calcium, phosphorus, trace elements (iron, zinc) and vitamins (D, E and K) that are essential and required to meet their daily recommended nutritional requirements.[5,12]

VLBW neonates need higher calories, protein and minerals to achieve adequate catch-up growth.[13] The goal of nutritional management of ELBW and VLBW neonates are preservation of endogenous body stores, achievement of postnatal growth similar to intrauterine weight accretion and body composition, and maintenance of normal physiological and metabolic process concomitant with minimizing complication and side effects [14] and inability of meeting these goals through parenteral nutrition or by providing enteral feedings through exclusive human milk resulting in significant growth failure. Hence,

these neonates need multi-nutrient supplementation till they reach term gestation (40 weeks postconceptional age).[5]

Adequacy of delivery of nutrients could also be altered because of immature feeding skills. Oral feeding in neonatal period requires the co-ordination of suction, swallowing and breathing movements which develops at 34 weeks of gestation. Before this, it is necessary to use enteral nutrition measures to continue feeding, so human milk (Expressed human milk) is provided by katori, palladio, spoon feeding, Oro-gastric tube.[7] The approach to successfully initiating and then advancing enteral feeding is to use the 'minimal enteral feeding' (MEF) strategy also known as trophic feed.[15] MEF i.e initiation of enteral feedings at small dosages of 5–25 ml/kg/day. MEFs also termed as trophic feeds and shows positive impact on gut through stimulating many aspects of gut function.[16]

On the basis of literature, exclusive breastfeeding with unfortified human milk results in poorer rate of growth and nutritional deficit; therefore, human milk should be fortified to increase its nutritive content to meet the requirement of these vulnerable neonates.[17] Human milk fortifier added to human milk is developed from bovine milk to supplement key nutrients with main emphasis on protein, calcium, phosphorus, and vitamin D [11] It has been suggested that higher protein intake is beneficial for premature growth.[9] The addition of HMF to EBM has shown positive effect on growth. But some studies have also shown that fortification with HMF can result in increase in milk osmolality leading to feed intolerance.[18]

The neonatal form of chronic lung disease (CLD), also termed as bronchopulmonary dysplasia (BPD), is also a topic of discussion nowadays as also related to prematurity and very low birth weight. BPD results from the impact on the immature neonatal lung and is associated with a significantly increased risk for pulmonary impairment persisting into adulthood. Minimizing long-term pulmonary impairment, and neurologic complications associated with BPD has become the

main focus of perinatal care Risk factors of BPD includes, prematurity, inadequate nutrition, and oxygen (leading risk factor). Oxygen is also the main treatment option in neonates suffering from impaired lung growth when diagnosed with BPD. Oxygen is like a sword, it has two faces, it also the treatment modality in neonates with BPD with respiratory distress, but also one of the many risk factors for BPD and ROP (Retinopathy of prematurity). Nutrition plays a critical role in the prevention and management in neonates with BPD. As malnutrition seems to worsen BPD by compromising lung development and function. Feeding difficulties in these neonates can further affect nutrition. In BPD neonates, the energy requirements increase because of increase work of breathing along with the lung damage/repair process. This energy should be provided in restricted fluid intake, since fluid overload may cause pulmonary edema, which further compromise lung compliance and increase airway resistance. In neonates with chronic lung disease, a high-fat diet theoretically produces lower rates of carbon dioxide production than a diet with a lower fat and higher carbohydrate content.[19] Inadequate nutrition also leads to development of ROP (Retinopathy of prematurity) which again a matter of major concern. As ROP is a leading cause of childhood blindness. Prevention of malnutrition, judicious use of ventilation and oxygen therapy are the promising factors that may reduce the incidence of BPD and severity of ROP in these high-risk neonates.[20] ROP can usually be effectively treated if diagnosed within window period.[21]

Fat in human milk supplies a major caloric content, but ability to absorb fat is poor in VLBW neonates due to immaturity of liver and decreased bile synthesis.[22] MCT i.e., medium chain triglyceride is proven to be a good source of fat and adequate energy. Medium chain triglyceride oil used for the treatment of fat absorption and found to be the major source of energy in VLBW neonates and the increase in weight gain was comparably more as per energy intake. It is great source of energy for neonates who need fluid restrictions as it easily gets converted into energy from fatty acid after absorption. It provides

sufficient energy in VLBW neonates who need fluid restrictions (Neonates with PDA, BPD). It is preferred over other triglyceride as it easily diffuses from GIT to portal system without modification unlike long chain triglycerides and improves fat absorption in VLBW neonates.[23] MCT oil enhances monosaccharide and amino acid absorption. Human milk fortified with MCT showed increase in weight gain and also showed increased calcium absorption.[24] Some studies have used coconut oil instead of MCT oil with human milk for weight gain. Question is, is MCT the same as coconut oil? No. Even if it's made from coconut, it is going through additional refinement (fractionation) to isolate the medium chain triglycerides.

Most of the studies carried out previously regarding fortification is mainly on protein-based fortifiers and are cross-sectional studies. More studies have told the effect of MCT oil by massaging it on VLBW neonates and not by using it in these neonates' feeds. We have conducted this unique study to find out the efficacy of the use of MCT oil in EBM along with HMF (though MCT oil is off labelled and not recommended as per WHO guidelines). In this study, we studied the weight gain pattern in VLBW neonates receiving EBM fortified with HMF in one group and EBM fortified with HMF and MCT oil in the other. We also compared that in which group there were more incidences of BPD, ROP, IVH, Feed intolerance and sepsis.

AIMS & OBJECTIVES

❖ **Primary objective -**

- To compare the weight gain using HMF+ MCT oil v/s HMF alone to breast milk.

❖ **Secondary Objective -**

- To Compare the duration of stay in hospital
- To Compare the incidence BPD, ROP, NEC, IVH, Sepsis

REVIEW OF LITERATURE

Poor weight gain and growth is a common and considerable problem in VLBW neonates. It starts at the time of admission and continues after discharge resulting in failure to thrive and wasting in the first year of life. Most of the neonates with very low birth weight are premature and are prone to get significant illnesses in the first few weeks of life. Adaptation to extrauterine life is an energy-consuming process due to increased losses from respiration, metabolism, thermoregulation, tissue synthesis, and activity.[25] During this adaptive period, VLBW neonates might lose up to 15 to 20% of their birth weight (BW). VLBW neonates need higher fluid to overcome insensible water losses in the initial few weeks of life. And if nutrition is being delayed, then the effect on heath is profound. Additionally, the time to return to Birth weight is a critical determinant of ultimate growth percentile at discharge. If supplementation of nutrition delays, it could lead to several complications. [26] Premature neonates have immature organs and because of the gut immaturity, they are more likely to experience feed intolerance necessitating adequate monitoring and treatment. The mortality rate of VLBW neonates have come down in last 20 years. All this has come in grip with advanced healthcare facilities. A lot of new techniques are adopted to handle such fragile neonates, including strategies to provide nutrition, early initiation of enteral feeding, supplements to milk, and intravenous nutrient solutions.[27] Adequate feeding led to reduction of mortality rate and Optimal feeding led to subsequent growth and development. Data suggests that we have made remarkable improvement in neonatology but we are lagging in achieving appropriate weight gain and maintain immediate postnatal growth even after adopting new strategies.[27] The weight of VLBW neonates remaining below 10th centile at the time of discharge, leads to postnatal growth restriction.[28]

Study done by Martins EC et al (2009) compared the weight and height gain and the frequency of clinical complications in preterm new born weighing less than 1,500 g, exclusively fed human milk or fortified

human milk until reaching 1,800 g.15 Prospective double blind randomized controlled trial involving 44 preterm neonates weighing <1,500 g at birth and ≤34 weeks of gestational age were included. Daily weight gain, weekly length and head circumference gain, nutritional variables and clinical complications were compared. Human milk fortification resulted in better growth, the weight gain was 24.4 and 21.1 g/day (p = 0.075). There were no significant clinical complications.[29]

Protein fortifiers to increase the nutritive content of human milk are usually commercially available, and are available in liquid or powder forms. They also contain additional micronutrients and electrolytes, and can be bovine or human milk-based. They are mixed with human milk, and fed to the preterm infant once they begin to tolerate enteral feeds. Protein based fortifiers are used as they are expected to improve postnatal growth and development by providing essential amino acids and energy for tissue growth, and by interacting with endocrine systems, such as the insulin-like growth factor I (IGF-1) system. IGF-1 plays an important role in growth and development of body.[30]

Lucas' data demonstrate that proteins are the key nutrients for early nutritional benefits.[31]

Protein based fortifiers are used as they are expected to improve postnatal growth and development by providing essential amino acids and energy for tissue growth, and by interacting with endocrine systems, such as the insulin-like growth factor I (IGF-1) system. IGF-1 plays an important role in growth and development of body.[32]

Study by Loui A et al (2013) showed the impact of use of high enteral protein nutrition strategy in human milk-fed neonates. Study was done on 43 neonates who weighed < 1500 g with mean gestation of 27+6 weeks and a mean birth weight 984 g (675/1130). These neonates revealed a weight gain of 14.9 g/kg/day (12.9/15.7), an increase in head circumference of 0.82 cm/week (0.75/0.90) and an increase in body length of 1.13 cm/week (0.98/ 1.23) from birth to day 70 of life,

thus concluding that high protein nutrition enables to achieve growth rates similar to fetal growth weight gain and head growth of VLBW neonates during the first 5 weeks of life.[32]

Study carried out by Hellström A et al (2016 June) showed that there is a reciprocal relationship between IGF-1 and dietary protein in preterm neonates at 30 weeks of postmenstrual age. Low protein levels are associated with low IGF-I concentrations leading to lower lean mass. Prolonged low serum IGF-1 levels predisposed to increase risk of multiple major neonatal morbidities such as bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), poor brain development and generalized growth retardation in extremely premature neonates and have a significant impact on long-term health. Therefore, the addition of protein to human milk is expected to raise IGF-1 concentrations, decrease fat mass accretion, and limit the initial growth failure of preterm neonates.[33]

Study done by Mukhopadhyay K et al analyzed the effects of human milk fortification on 166 neonates (Neonates weighing ≤1500 grams and ≤34 weeks of gestation) on short term growth and biochemical parameters in preterm very low birth weight (VLBW) appropriate for gestation (AGA) and small for gestation (SGA) babies. Primary outcome measures were Short-term growth (daily weight, length and head circumference (HC) weekly) till discharge or 2 Kg. Fortification resulted in better growth in preterm VLBW babies as compared to control group.[13]

Study done by Lucas A et al showed that neonates who weighed less than 1850 gm and on feed fortifications had better neurodevelopment and growth at 18-months follow-up without adverse short-term clinical or biochemical consequences. A randomized controlled trial included 275 preterm neonates with a mean gestation of 29.8 ± 2.7 wk (range: 23-36 wk) and a mean birth weight 1284 ± 3 1 4 g. Daily weight gain, weekly length and head circumference gain, nutritional variables and clinical complications were compared. Neonates were studied until they

were discharged or reached 2000 g body weight, whichever was sooner and were followed up at 9 and 18 months of corrected gestational age. There were no significant growth advantages with fortification; although, when breast milk exceeded 50% of intake, fortification promoted faster weight gain (an advantage of 1.6 g/kg/ d; 95% CI: 0.1, 3.1; P < 0.05). Developmental scores at 18 months were slightly but not significantly higher in the fortified group. This study confirmed that breast milk fortifiers can improve short-term growth (when breast milk intakes are high).[34]

Study done by Brown JVE (2016) showed that fortification of expressed breast milk with HMF increases the nutrient content of the milk without compromising its other beneficial effects (such as reduction of necrotizing enterocolitis, infections, etc.). Experimental studies have shown that the use of fortified human milk results in net nutrient retention that approaches or is greater than expected intrauterine rates of accretion in preterm neonates. Though there were concerns about the increase in osmolality; clinical studies have not shown any significant adverse effects following fortification of human milk. The Cochrane review on fortification found improvement in weight gain, linear and head growth without any increase in adverse effects such as necrotizing enterocolitis (NEC).[35]

Use of a Liquid human milk fortifier in an unrestricted NICU population resulted in an increase in clinical complications within a high-acuity NICU, including metabolic acidosis and poor growth. Although further research is needed to assess outcomes among neonates with a variety of clinical acuities, gestational ages, and weights to confirm these findings, based on this experience, caution is urged to avoid potential risks.[10]

Study done by Colaizy TT and et al (2012) demonstrated that 97% of neonates received human milk, 51% received > 75% of all enteral intake as human milk. Those fed >75% human milk had a greater negative change in weight z-score from birth to discharge compared to

neonates receiving < 75% (-0.6 vs, -0.4, p = 0.03). In neonates receiving > 75% human milk, there was no significant difference in change in weight z-score by milk type (mother's own vs. donor). Our current standardized fortification of human milk may not adequately support early postnatal growth.[36]

Study done by Moya F et al did study in Oct, 2012 in which preterm neonates with BW <1250 grams were randomized to get LHMF vs powder HMF (20% higher protein in LHMF). At 28 days, the LHMF had achieved a significantly higher weight, length, head circumference, and linear growth rate than the control HMF (P = .004, P = .003, P = .04, and P = .01, control HMF (P .004, P .003, P .04, and P .01 respectively).[37]

Study done by Book LS et al (1975,) shows that Osmolality is a critical determinant of feed tolerance.[5,6] Milk fortification results in significant increase in osmolality.[5,6] Feed intolerance may result in the reduction in nutrient intake which can explain lower weight gain compared to formula in VLBW neonates. An association between hyper-osmolar feeds (400 mOsm/ kg) and NEC has also been reported.[38]

Erin Grace et al carried out a randomized controlled trial and compared the effect of fortification of human milk with HMF versus cow's milk-based fortifier in neonates who were born with gestation <34 weeks' or with birth weight <1500 g. It showed less risk of necrotizing enterocolitis (risk ratio 0.47, 95% CI 0.22 to 0.98) in neonates who were on human milk fortification than on cow milk's.[28]

Fat is an important source of energy and is important for certain biological compounds. It supplies unsaturated fatty acids (building material for cell membranes -especially in the nervous system and the retina of the eye). Cholesterol builds the structure of cell membranes, precursors of bile acids, some steroid hormones, and vitamin D3, also important for myelinization of the central nervous system. Thus, it is important during early development. Fats are also a carrier of A, D, E, K vitamins. As VLBW neonates are born with low fat content, therefore

they are provided with it exogenously. Studies have shown that absorption of the larger part of lipids (LCT) requires emulsification with bile whereas MCT (Medium chain triglycerides) are digested more easily as it does not require bile and lipase. MCT oil is used in nutrition of premature neonates due to high demand for energy. MCT is preferred over LCT as activity of gastric lipase in these neonates are insufficient.[39] Study carried out by Sulkers et al showed that prematurely born neonates fed with a formula with increased content of MCT, the increase of body mass was higher.[40] Improvement in the increase of body mass and increase of the skin fold thickness in neonates born with low body mass, induced by MCT formula, was observed by Vaidya et al.[41]

Study done by Verma GK et al. (2018) on analysis of data, showed that the weight gain of neonates who received HMF fortified maternal milk was 14.91 g/kg/day and overall fortified human milk has tremendous benefits in improving the growth and short-term outcomes for the premature infant. Mother's own milk has clear advantages due to its composition. Premature neonates need fortification of human milk to achieve growth as recommended. Based on the results of this study, we concluded that the supplementation with HMF, can result in a significant increase in growth (weight, linear and head growth).[5]

Daily body weight gains of neonates substituted MCT oil were statistically better than the control group in energy intake 70s to 120s Kcal/kg/day categories with the exception of 90s Kcal/kg/day category. To increase one gram of body weight, 5.2 kcal/kg/day and 5.8 kcal/ kg/day in MCT group and control group were needed respectively. Moreover, if it is hypothesized that MCT oil is not used as energy, only 4.5 kcal/kg/day in the MCT group are necessary to increase one gram of body weight. All these data clearly suggest that MCT oil is definitely utilized for the weight gain of very pre- mature neonates.[23]

Study by Yamada T, et al (1988) showed the efficacy of medium chain triglyceride (MCT) as an energy source in premature neonates.

neonates who were given 3 g/kg/day of MCT oil gained body weight better than the control group in spite of a smaller water intake. This was advantageous to neonates who need water restriction due to patent ductus arteriosus (PDA), bronchopulmonary dysplasia (BPD), etc. Also proved that MCT oil is rapidly absorbed and digested, by means of the '3C-trioctanoin breath test. The mean body weight gain was 19.7+/- 9.9 g/day in the neonates given MCT oil and 17.9+/-12.5 g/day in the control group. The difference is not statistically significant. Energy intakes were 110.4 k 14.3 kcal/kg/day in the MCT group and 1 1 1.1 * 17.3 kcal/kg/day in the control group, while water intake was 137.6k6.9 ml/kg/day and 158.3k18.9 ml/kg/day respectively. neonates who were given MCT oil received almost the same energy intake, whereas the water intake was less than in the control group. The body weight gain of neonatesreceiving MCT oil supplementation was better than in the control group in almost all daily energy intake categories, suggesting that MCT oil was utilized more efficiently than milk as an energy source.[23]

Study by ROY CC and et al demonstrated that MCT oil (Medium chain triglycerides) helped in absorption of monosaccharide and amino acid. After ingestion of milk-based formula supplemented with fortifiers (MCT and LCT) for one week, 16 preterm neonates, weighing 1,300 to 1,800 gm, were fed two isocaloric formulas i.e. (containing either medium-chain or long-chain triglycerides) for 15 days; the alternate formula was given for a second period of identical duration. It was seen that neonates who were receiving MCT had greater (P smaller than 0.01) percent fat absorption (83.4 leads to 97.1%) and weight gain (7.5 leads to 11.5 gm/kg/100 calories). Because lower percentage of fat absorption and weight gain was seen in group on LCT formula, secondary to hyperchloremic acidosis, the chloride content was adjusted to same as that of MCT and was confirmed, however there was a higher (P smaller than .01) percent retention of nitrogen using MCT when compared.[24]

Okamoto E, Muttart et al demonstrated failure of the resulting small increase in fat absorption incident to MCTs either to promote enhanced growth or to confer obvious clinical benefit. It does not support the increasing use of MCT formulas for routine feeding of preterm neonates.[42]

Alice L. Bashinsky concluded that for the development and progression of ROP, one of the important factors is extremely low birth weight and gestational age 30 weeks and under. There is a need of preventing ROP through optimal prenatal care. Reducing subsequent post-natal risk factors depends on optimal perinatal and postnatal care, as well as adhering to strict ROP screening guidelines. Recognizing and treating ROP in a timely fashion is critical for achieving the best visual outcome.[43]

Retinopathy of prematurity (ROP) is a retinal neo- vascular disease seen in preterm neonates. ROP can lead to retinal detachment and blindness if not detected and treated at the right time. Advancement in medical services has led to increased survival of preterm neonates but on the same hand has also increased the neonatal morbidities; one of which is ROP. Studies have shown that IGF-1 is needed for normal retinal vascularization and it also influences VEGF- induced retinal vascular growth. Levels are low in preterms leading to higher risk of development of retinopathy. IGF-1 is regulated by calorie and protein intake, so it is seen that postnatal growth can also be used as a surrogate measure for serum IGF-1.

Extreme preterm neonates who weigh < 1000 gm are vulnerable to have low energy intake during their early neonatal intensive course, which has been associated with poor weight gain in the first 4 weeks of life and suboptimal postnatal weight gain in the first 2 weeks of life. It has also been found to be an independent risk factor for ROP. Keeping the possibility that the neonates who developed Type 1 ROP were at a higher risk of low energy intake during the immediate to early

postnatal period which possibly resulted in IGF-1 mediated vascularization arrest.[44]

Randomized control study was done by Khan SA on 120 stable neonates with gestation more than 30 weeks and weighing between 1800-2500 gm. Neonates were divided into three groups which include daily massage with coconut oil, daily massage with Medium Chain Triglyceride oil and daily massage with Medium Chain Triglyceride oil+ oral intake of Medium Chain Triglyceride oil. Total 120 neonates were enrolled, 40 neonates in each group. All the groups were comparable and it was seen that there was significant weight gain in group B (p-value-0.001) than group A (69.3%) since birth after 3 months of therapy. In comparison between group B and group C there was significant weight gain in group C (p-value-0.018) (88.7%) in comparison to group B. Similarly group C neonates had better weight gain than group A (p-value-0.001). Study concluded that MCT massage + oral intake has significant effect on weight gain.[45]

Factors leading to growth failure in VLBW babies is inadequate nutrition. Although, higher amounts of protein, sodium, chloride, and magnesium are present in preterm human milk but these levels are still below recommendations. Joshi S et al studied the effect of fortification of human milk for weight gain. Using Prospective cohort study, the babies were assigned to group 1, 2 and 3 in serial order. Sample size in each group was 75. Group1- EBM with lactodex-HMF, Group 2- EBM with lactodex-HMF and MCT, Group3-EBM with lactodex-HMF and coconut oil. Parameters such as physical growth (weight, length and head circumference) were studied over a period of two months and they noticed that there was significant weight gain in each group but no additional benefit was seen using MCT or coconut oil in addition to Lactodex- HMF on the physical growth of VLBW babies.[10]

MATERIAL & METHODS

This study was designed as randomized controlled trial and conducted in a setting of 30 bedded neonatal intensive care unit of Dayanand Medical College and Hospital, Ludhiana, Punjab between 1st jan,2020 to September 2021

DURATION OF STUDY: One year and 9 months

STUDY DESIGN: Non-blinded, Randomized controlled trial

STUDY POPULATION:

INCLUSION CRITERIA:

- All VLBW neonates admitted in Neonatal intensive care unit
- Both inborn and out born neonates included in the study.
- These neonates accepting feed volume more than 100ml/kg/day
- Informed written consent received from the parents.

EXCLUSION CRITERIA:

Following patients were excluded from the study:

- Who were not accepting feed volume of 100 ml/kg/day
- Neonates who died in NICU
- Neonates who took discharge against medical advice
- Who had major surgical conditions
- Who had major congenital anomalies
- Who had chromosomal abnormalities
- Who had absented diastolic flow/ Reversal of end diastolic flow
- Whose parents/guardian did not give consent

Outcomes:

Primary outcome:

- To compare the weight gain using HMF+ EBM + MCT oil v/s HMF + EBM

Secondary outcome:

- To compare the duration of stay in hospital

- To compare the incidence bronchopulmonary dysplasia, retinopathy of prematurity, feed intolerance, intraventricular hemorrhage, sepsis

Randomization and Allocation Concealment:

A Computer-generated random number sequence was generated by a person not involved in the study, using strata 12 version. Allocation concealment was ensured using sequentially numbered, opaque, sealed and stapled envelopes that were opened by the primary resident available when VLBW neonates reached to feed volume @ 100ml/kg/day. It was open labelled, non-blinded trial

Selection of cases and Intervention:

VLBW neonates in NICU on reaching 100 ml/kg/day of feeds were enrolled and stratified into AGA and SGA according to intrauterine growth. They were then randomized to breast milk along with HMF or breast milk with HMF and MCT oil.

Group A: Receiving Expressed human milk + Commercial Human milk fortifier **(**Lactodex-HMF (Raptakos, Brett and Co. Ltd.):-1 g sachet was added to 25ml of EBM.

Group B: Receiving Expressed human milk + Commercial Human milk fortifier + Medium chain triglyceride oil (MCT oil)

(In addition to lactodex-HMF, medium chain triglyceride was added (Simyl MCT oil: Neonates received MCT oil (Fssai Lic.No: 10014022002634)

Neonates were given EBM every 2-3 hourly. EBM included own mothers' milk and donor human milk. Feeds were progressed at the rate of 20-25 ml/kg/day. These neonates were fed with EBM with HMF v/s HMF with MCT oil. Dose delivered was 0.2ml of MCT oil in 25 ml of EBM and 1 g HMF in 25 ml EBM and this dose was kept constant throughout the study period. The fortified EBM was given till 40 weeks of corrected gestational age. Before taking intervention in respective groups, written informed consent taken from guardian/ parents. The

intervention was given through nasogastric tube till 1.2 kg and paladai (a beaked cup used locally). They were discharged at corrected gestational age of > 34 weeks. In case of discharge before 40 weeks, the intervention was continued at home. The discharge summary included proper instruction. Compliance was checked during follow up visit in OPD. Daily weight monitoring was done using digital electronic scale (Easy care) (fig no.2) after removal of clothes and diaper (fig.3). The weighing machine was corrected for zero error before measurement. Serial measurement of weight was done on the same weighing scale. These babies were serially followed for weight gain till their hospital stay and then followed them for 3 months.

As per standard guidelines, Fortifier (HMF/ HMF +MCT oil) were mixed with EBM before it is administered to neonates. Neonatal nurses were mixing EBM with HMF or HMF along with MCT as advised. Every 2 hourly EBM/donor human milk was fortified. This fortified EBM was then fed to neonate via feeding tube/ katori spoon feeding.

All the mothers were counselled and supported in expressing their own milk for feeding their neonates and it was initiated within hours of delivery so that neonate got benefits of colostrum.

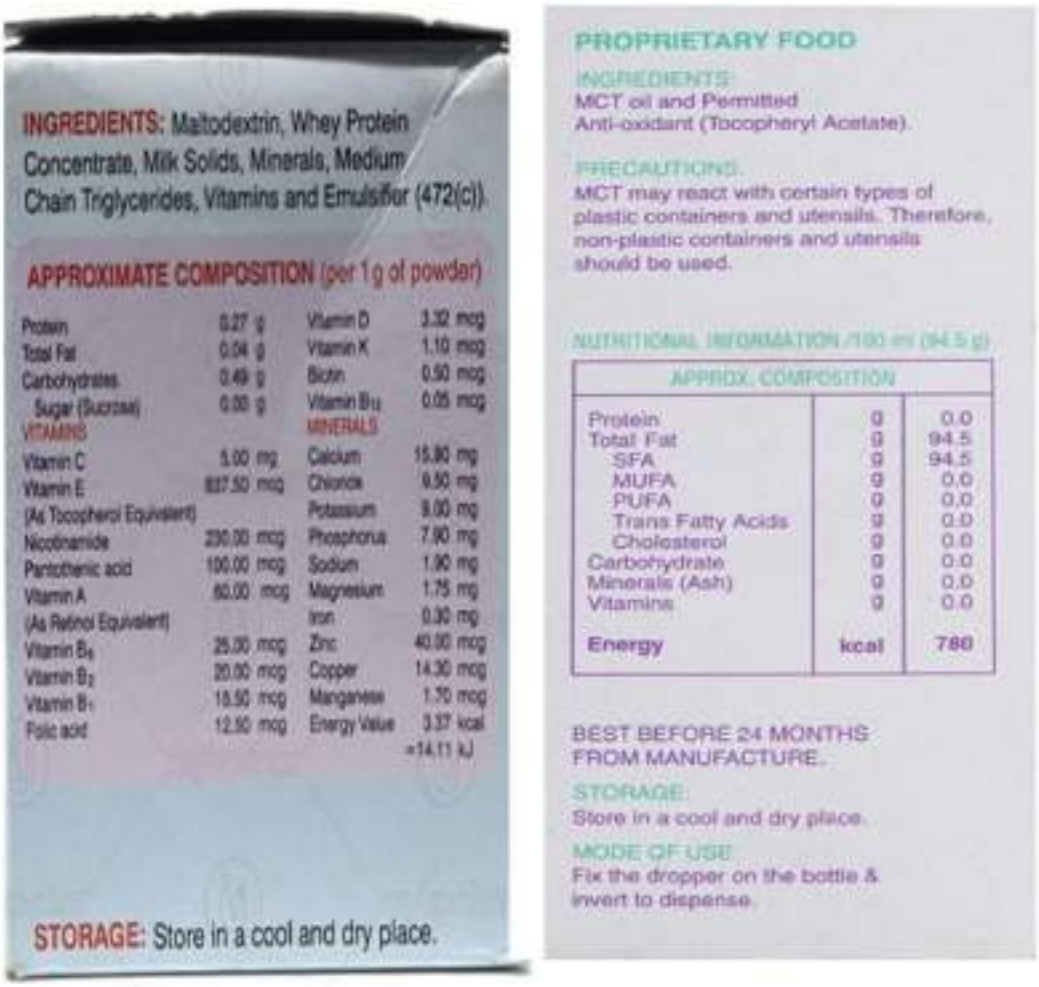

INGREDIENTS: Maltodextrin, Whey Protein Concentrate, Milk Solids, Minerals, Medium Chain Triglycerides, Vitamins and Emulsifier (472(c)).
APPROXIMATE COMPOSITION (per 1 g of powder)
Protein 0.27 g
Total Fat 0.04 g
Carbohydrates 0.49 g
Sugar (Sucrose) 0.00 g
VITAMINS
Vitamin C 5.00 mg
Vitamin E 837.50 mcg
(As Tocopherol Equivalent)
Nicotinamide 230.00 mcg
Pantothenic acid 100.00 mcg
Vitamin A 60.00 mcg
(As Retinol Equivalent)
Vitamin B6 25.00 mcg
Vitamin B2 20.00 mcg
Vitamin B1 18.50 mcg
Folic acid 12.50 mcg
Vitamin D 3.32 mcg
Vitamin K 1.10 mcg
Biotin 0.50 mcg
Vitamin B12 0.05 mcg
MINERALS
Calcium 15.80 mg
Chloride 9.50 mg
Potassium 9.00 mg
Phosphorus 7.90 mg
Sodium 1.90 mg
Magnesium 1.75 mg
Iron 0.30 mg
Zinc 40.00 mcg
Copper 14.30 mcg
Manganese 1.70 mcg
Energy Value 3.37 kcal
=14.11 kJ
STORAGE: Store in a cool and dry place.
PROPRIETARY FOOD
INGREDIENTS
MCT oil and Permitted
Anti-oxidant (Tocopheryl Acetate).
PRECAUTIONS
MCT may react with certain types of plastic containers and utensils. Therefore, non-plastic containers and utensils should be used.
NUTRITIONAL INFORMATION /100 ml (94.5 g)
APPROX. COMPOSITION
Protein 0 0.0
Total Fat 0 94.5
SFA 0 94.5
MUFA 0 0.0
PUFA 0 0.0
Trans Fatty Acids 0 0.0
Cholesterol 0 0.0
Carbohydrate 0 0.0
Minerals (Ash) 0 0.0
Vitamins 0 0.0
Energy kcal 780
BEST BEFORE 24 MONTHS FROM MANUFACTURE.
STORAGE
Store in a cool and dry place.
MODE OF USE
Fix the dropper on the bottle & invert to dispense.

Fig No.1: Composition of Lactodex HMF and Simyl MCT oil

Fig no. 2: weighing machine

Fig no. 3: Discrption of daily weight monitoring by placing naked baby on weighing machine

The primary outcome was to compare the weight gain using HMF alone or HMF with MCT oil in EBM.

The secondary outcomes were to compare the length of hospital stay, feed intolerance (defined as vomiting, abdominal distension > 2 cm from baselines, increased aspirate), Bronchopulmonary dysplasia (BPD)- defined as the need for supplemental oxygen dependence at 36 weeks' PMA. Moderate BPD was defined, based on the diagnostic criteria of the National Institute of Child Health and Human Development Workshop severity, which requires provision of oxygen for more than 28 days, and an addition of <30% oxygen at 36 weeks' PMA. Severe BPD was defined as the need for oxygen for >28 days plus ≥30% oxygen and/or positive pressure at 36 weeks' PMA, according to National Institute of Child Health and Human Development criteria.[46] Intraventricular haemorrhage (IVH) grade > 2, Retina of prematurity (ROP) defined as Vaso- proliferative disorder of retina. Neonates who were born =/< 32 weeks or with weight <1500gm were at risk of development of ROP were also timely assessed during the hospital course of these neonates, NEC was defined based on a modified Bell staging classification grade ≥II. LOS was defined as a positive blood culture from a peripheral artery or vein after 5 days of life, in symptomatic neonates with antibiotic treatment.

The primary outcome variable for this study was weight gain (g/kg/day) from the day of enrolment till discharge. The study subjects were followed up in high-risk clinic for 3 months.

Secondary outcomes:

For ROP screening, every week, an ophthalmologist visits the NICU and the findings were noted down (included detail zoning, stage, extent in term of clock of hours of any ROP and the presence of any pre-plus or plus disease). These notes also include a recommendation of next examination.

For IVH, Screening bedside USG cranium was performed within 72 hours of birth and then weekly screening was continued till their hospital stay.

Calculation and ordering of fortifier dose:

- 1g of HMF was mixed with 25ml of EBM in group A. This was delivered, the fortifier calculated and ordered by the resident on the duty

  For example, the calculation for an neonate weighing 1.2 kg required 120ml/kg/day and fed 2 hourly is as followed:

  - Calculate total intake:
    1.2 x 120ml/kg/day(ml/day) =144 ml

  - Calculate total HMF required (gm/day) where 1 gm HMF is to be delivered /25 ml of EBM:
    144 /25=5.76 g

  - Calculate HMF required per feed (g/feed)
    5.76/12=0.4 g

- 0.2ml of MCT was mixed along with 1g of HMF in 25 ml of EBM in group B. This was delivered and fortifier calculated and ordered by the resident on duty.

- Total energy and protein delivered per day through fortification 19.411kcal/kg/day and 1.55 g/kg/day respectively.

Fig no. 4: HMF and MCT oil with EBM before fortification

Fig no.5: Fortification of EBM with HMF

Fig no. 6: Fortification of EBM with MCT oil

Masking: Non blinded study

Sample size calculation:

We calculated the sample size as per study by Vaidya et al with the difference in weight gain of 5 g/kg/day and power of study- 80 and alpha error-5 (using formula E= Mean difference / SD, n=16/ (E x E)). Adjusting for 20% lost to follow up, an additional nine cases were needed. The total sample size was estimated to be 90 (45 in each arm)

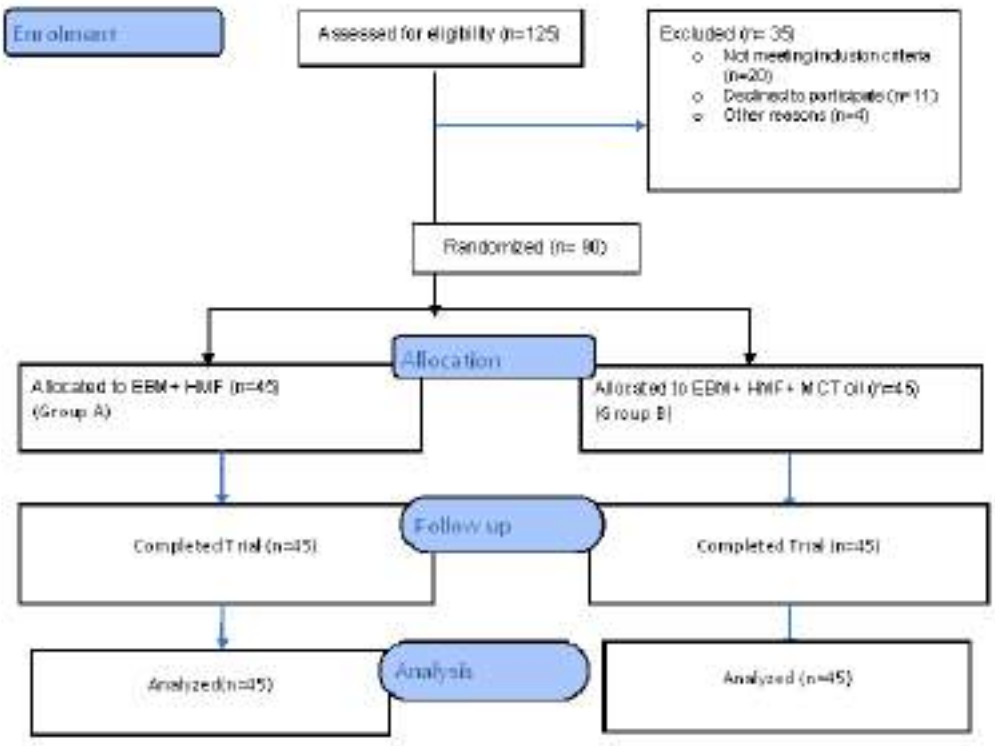
Statistical Analysis:

Data described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups done using Student t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. For comparing categorical data, Chi square ($\chi 2$) test performed and exact test was used when the expected frequency is less than 5. A probability value (p value) less than 0.05 considered statistically significant. All statistical calculations done using SPSS (Statistical Package for the Social Science) SPSS 26 version statistical program for Microsoft Windows.

OBSERVATION AND RESULTS

This prospective, randomized controlled trial study of 1 year and 9 months duration conducted on neonates who weighs less than 1500g admitted to Neonatal intensive care unit (NICU) of tertiary care multi-specialty teaching hospital (DMCH, Ludhiana). This was conducted to find out the efficacy of fortification of expressed human milk with MCT oil. HMF common to both groups as it has proven role in physical growth. During this time, 125 neonates were enrolled and 90 met the inclusion criteria and became part of the study. 90 neonates were randomly assigned to two groups. Sample size was 45 in each group.

Table-1 Study flow



Demographics and clinical characteristics of subjects:

Table-2: Distribution of subjects on basis of gestation

All the neonates who weigh < 1500 g were included in the study, the

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%Age	No. of cases	%Age			
Gestation (weeks) group	< 30	15	33%	19	42%	34	0.756	0.384
	> 30	30	67%	26	58%	56		

distribution of subjects according to gestation as

As shown in table no 2, in our study, out of total 90 subjects, 34 were <30 weeks with 15 (33 %) in group A (HMF+ EBM) and 19 (42%) on (HMF+MCT+EBM) and rest 56 with gestation > 30 weeks 30(67%) on (HMF+ EBM) and 26 (58%) on (HMF+MCT+EBM).

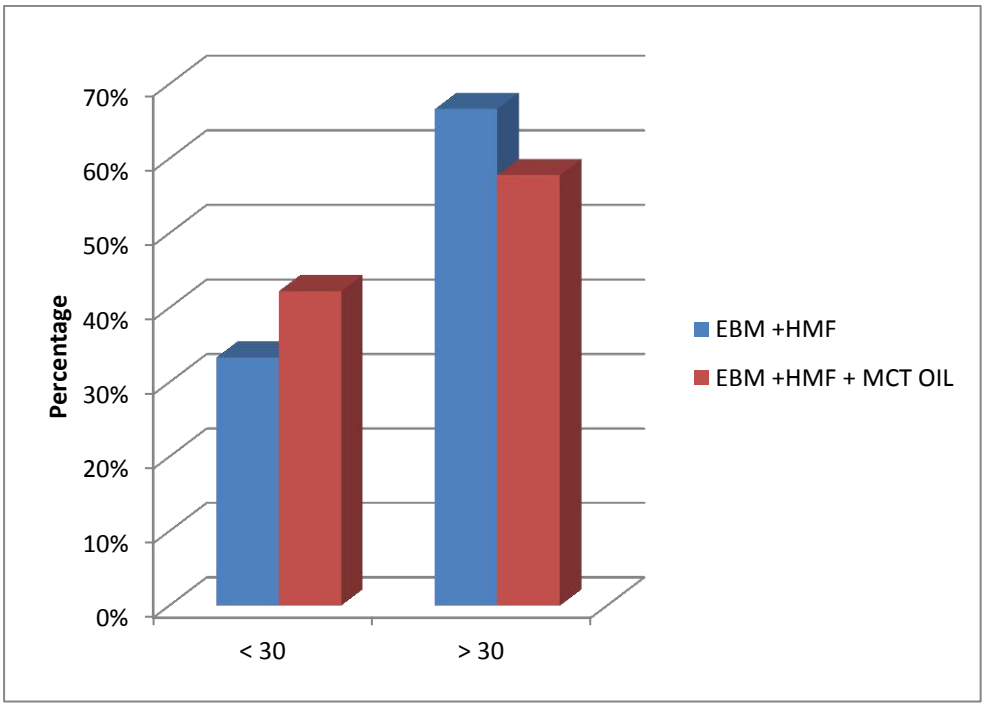


Fig no. 7: Distribution of subjects on basis of gestation

Table- 3: Gender distribution of the study

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age			
Gender	female	17	38%	17	38%	34	0.000	1.000
	male	28	62%	28	62%	56		

As shown in table 3, in our study group, out of 90 subjects, there were total 34 female and 56 were males, Out of 34, 17 were in group A and 17 in group B, whereas 28 in group A and 28 in group B

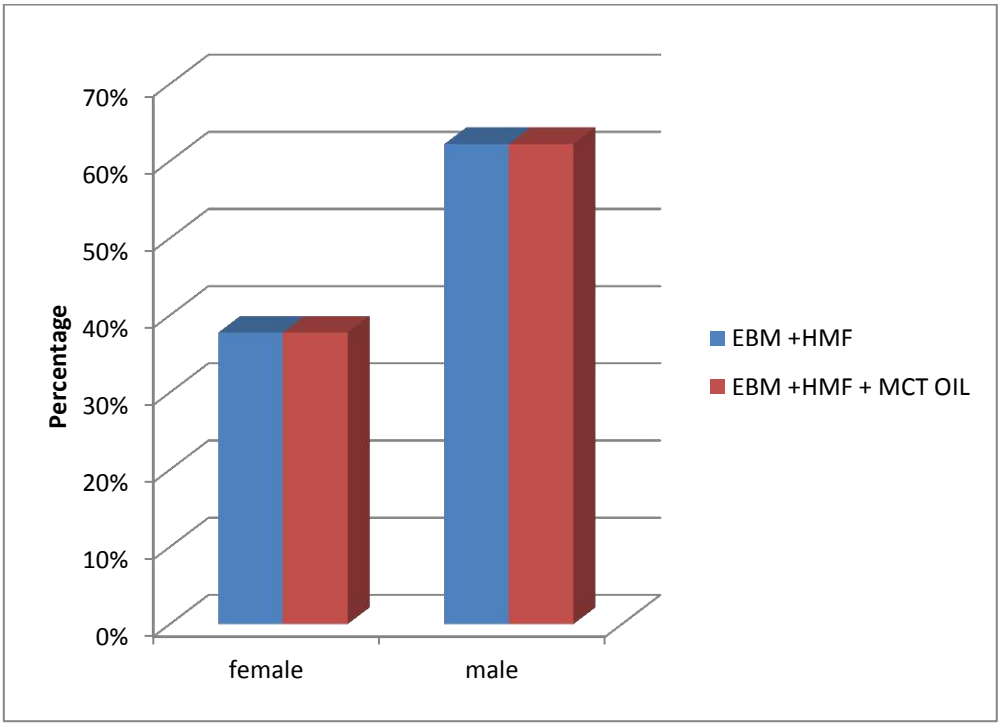


Fig no.8 : Gender distribution of subjects

Table-4 Baseline characteristics of the subjects

	EBM +HMF		EBM +HMF + MCT OIL		t	p-value
	Mean	SD	Mean	SD		
Duration of hospital stay(days)	33.84	15.84	33.62	18.33	0.062	0.951
Gestation (weeks)	30.24	2.23	29.51	2.61	1.434	0.155
Birth weight in Grams	1167.56	205.47	1162.78	202.83	0.111	0.912
APGAR Scores (for inborn) at 1min	6.45	1.15	6.50	1.37	-0.175	0.862
APGAR Scores at 5 min	8.28	0.75	8.21	0.91	0.343	0.732
Duration of ventilatory support(days)	4.81	2.84	7.13	4.66	-1.871	0.070
Birth weight(gm)0	1170.89	208.22	1156.44	199.12	0.336	0.737

The above table depicts the mean duration of hospital stay was 33.84 in Group A whereas 33.62 in group B. The mean gestation in weeks was 30.24 in group A and 29.51 in group B. whereas mean birth weight was 1167.56 g in group A and 1162.78 g in group B. The duration of ventilatory support was 4.81 days in group A whereas in group B it was 7.13 days. The mean birth weight in group A was 1170.89 g whereas in group b was 1156.44 g. Table no.3 summarized that all the baseline characteristics of the study were comparable but none of them showing p value <0.05. i.e. not statistically significant.

Table-5: Distribution of subjects on basis of growth status:

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%Age	No. of cases	%Age			
GROWTH STATUS	AGA	33	73%	32	71%	65	0.055	0.814
	SGA	12	27%	13	29%	25		

Growth status was assessed using Fenton intrauterine growth chart. As shown in table no. 5 in our study, out of 90 neonates, 65 were AGA, out of which 33 (73%) were in group A and 32(71%) in group B, and 25 were SGA, 12 (27%) in group A and 13(29%) in group B.

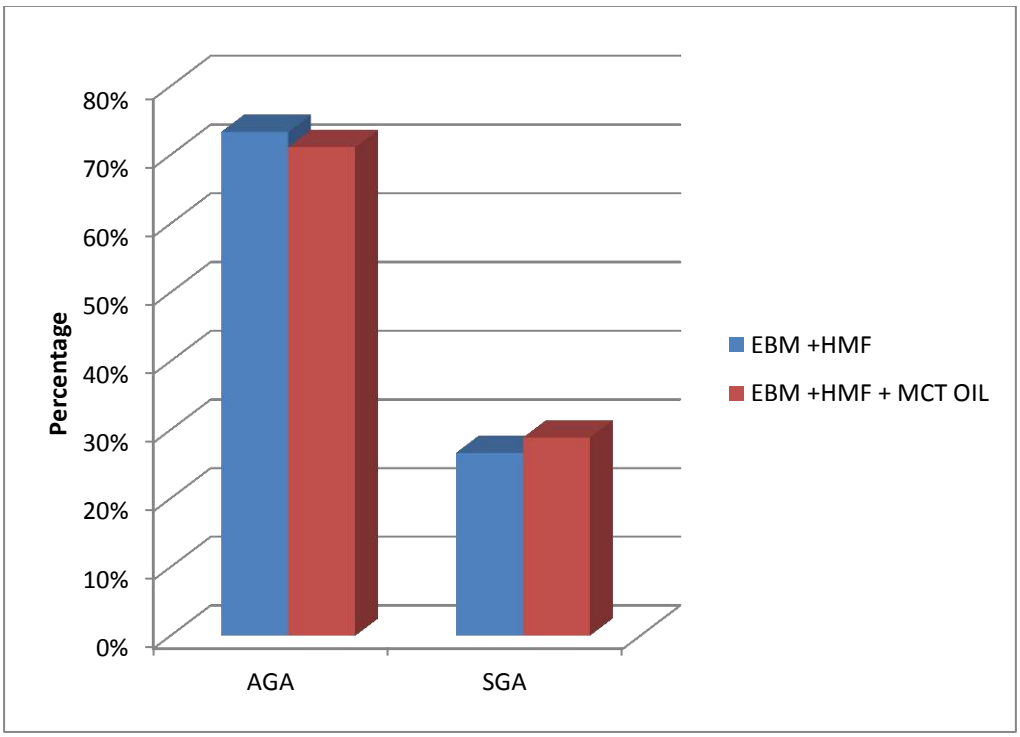


Figure no. 9: Growth status of subjects

Table-6. Distribution of subjects on basis of mode of delivery

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%Age	No. of cases	%Age			
Mode of Delivery	LSCS	39	87%	36	80%	75	0.720	0.396
	NVD	6	13%	9	20%	15		

As shown in table no.6, out of 90 neonates, 75 were born by Cesarean delivery and 15 were born by vaginal delivery. Out of which 87% of group A and 80% of group B born via LSCS.

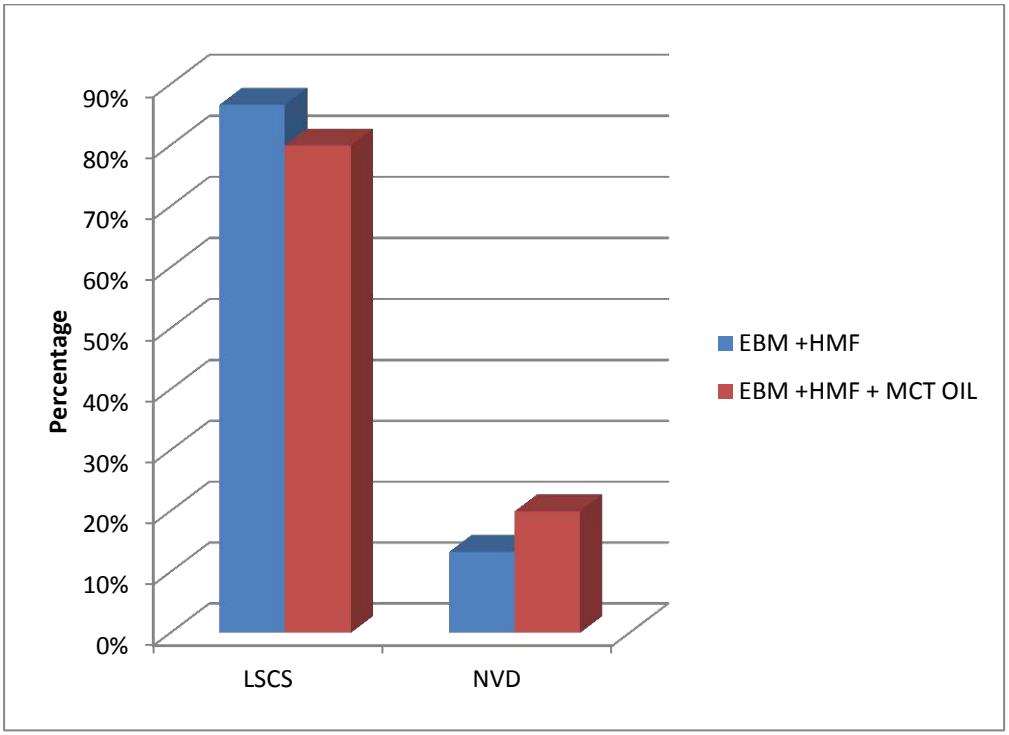


Fig no 10: Mode of delivery

Table 7: Characteristics of neonates on the basis of admission

REASON FOR ADMISSION		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age			
Prematurity	NO	0	0%	1	2%	1	1.011	0.315
	YES	45	100%	44	98%	89		
Respiratory symptom	YES	45	100%	45	100%	90		
Respiratory failure	NO	25	56%	36	80%	61	6.156	0.023
	YES	20	44%	9	20%	29		
Sepsis evaluation	NO	41	91%	35	78%	76	3.045	0.144
	YES	4	9%	10	22%	14		
Peri natal Asphyxia	NO	35	78%	39	87%	74	1.216	0.409
	YES	10	22%	6	13%	16		
Seizures	NO	45	100%	44	98%	89	1.011	0.315
	YES	0	0%	1	2%	1		
Hypoglycaemia	NO	44	98%	45	100%	89	1.011	0.315
	YES	1	2%	0	0%	1		

Hyper Bilirubinaemia	NO	45	100%	44	98%	89	1.011	0.315
	YES	0	0%	1	2%	1		
Metabolic evaluation	NO	45	100%	42	93%	87	3.103	0.242
	YES	0	0%	3	7%	3		
Small for gestational Age	NO	34	76%	33	73%	67	0.058	0.809
	YES	11	24%	12	27%	23		
Large for gestational age	NO	45	100%	45	100%	90		
Birth asphyxia requiring bag and mask evaluation	NO	22	49%	27	60%	49	1.120	0.397
	YES	23	51%	18	40%	41		
Need for ventilation	NO	24	53%	29	64%	53	1.147	0.284
	YES	21	47%	16	36%	37		
RDS	NO	0	0%	2	4%	2	2.045	0.153
	YES	45	100%	43	96%	88		
Need for surfactant	NO	23	51%	27	60%	50	0.720	0.396
	YES	22	49%	18	40%	40		
Apnoea of pre maturity	NO	21	47%	21	47%	42	0.000	1.000
	YES	24	53%	24	53%	48		
Feed intolerance	NO	21	47%	28	62%	49	2.195	0.138
	YES	24	53%	17	38%	41		

As summarized in table 7 and figure no. 12, the difference in clinical characteristics between two groups was statistically insignificant. (p value > 0.05, i.e., 0.315, 0.144, 0.409, 0.315, 0.315, 0.315, 0.242, 0.809,0.397, 0.284, 0.153, 1.000, 0.138) except the neonates with respiratory failure where the difference between two groups was statistically significant (p value =0.023)

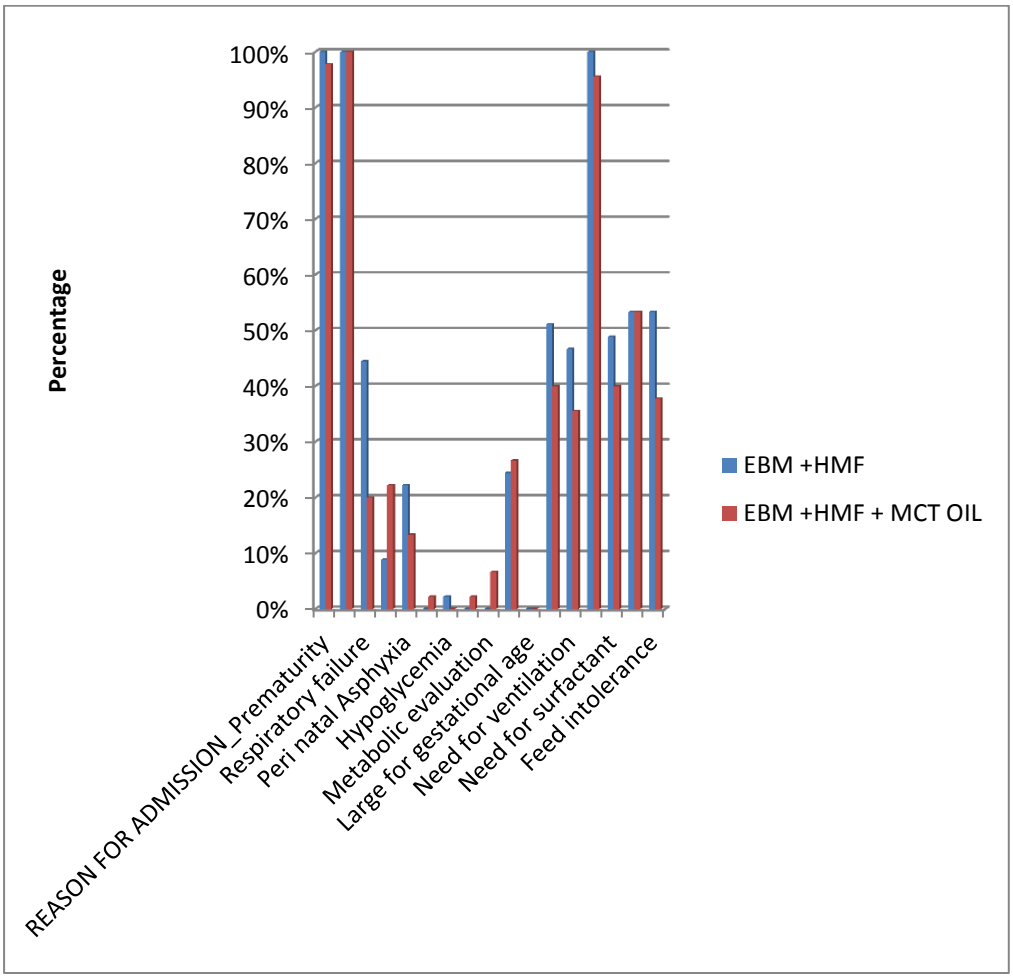


Fig no.11: Baseline characteristics of study subjects

Table-8: Neonates required inotropes during the study

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%Age	No. of cases	%Age			
Need for inotropes	NO	37	82%	41	91%	78	1.538	0.215
	YES	8	18%	4	9%	12		

Neonates having features of shock like feeble pulses, cold extremities, poor peripheral perfusion, CFT> 3 sec and required inotropic support were 12 out of 90 neonates. In the table above, Out of 12, 8 were in group A whereas 4 were in group B. Rest 78 neonates do not require inotropic support during hospital stay.

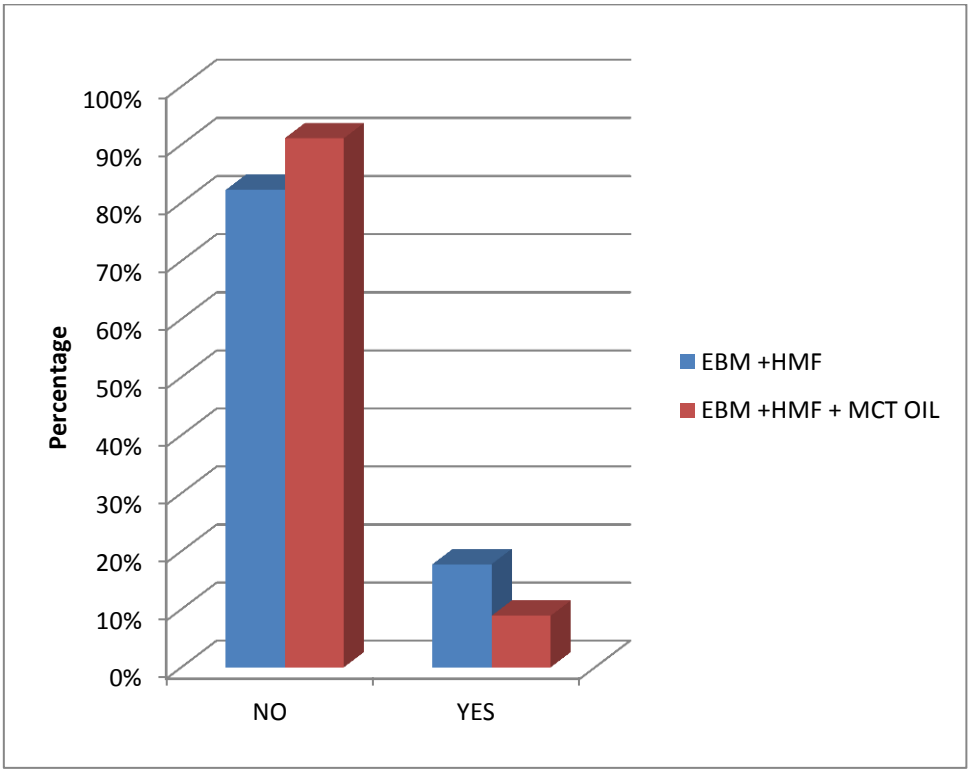


Fig no.12: Subjects requiring inotropes

Table-9: Distribution of subjects on the basis of requirement of CPAP

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%Age	No. of cases	%Age			
Need for CPAP	NO	2	4%	5	11%	7	1.394	0.238
	YES	43	96%	40	89%	83		

VLBW neonates are born usually <32 weeks and they have immature lung thus requiring CPAP. In our unit Bubble CPAP was being used. As shown in table no.9, there were total 83 neonates out of 90 who were on CPAP during their hospital stay and only 7 do not require CPAP. Out of 83, 43 were in group A whereas 40 were in group B. 7 neonates do not require CPAP.

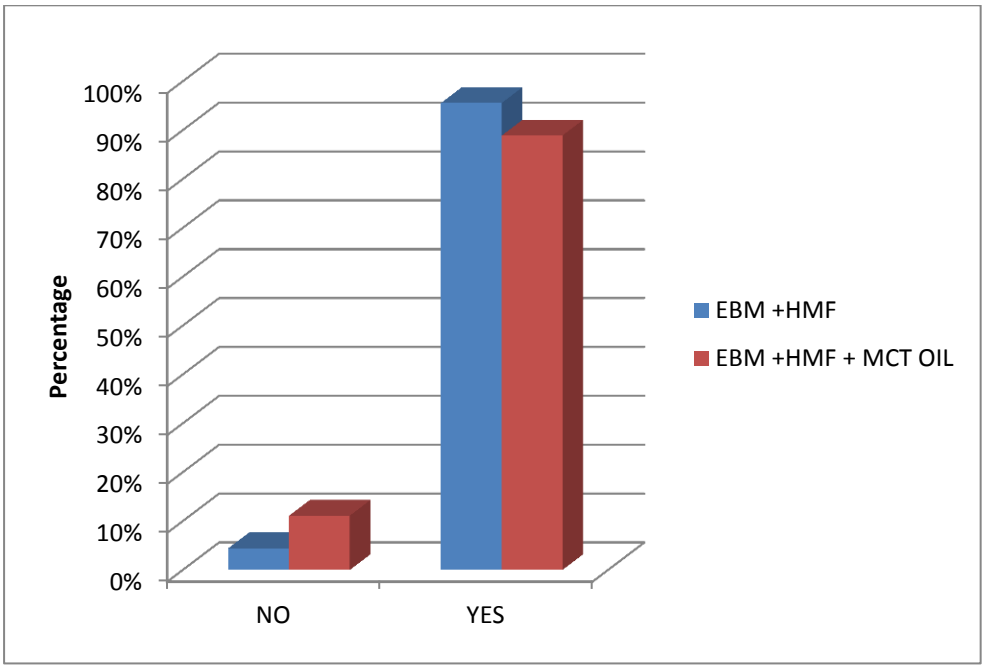


Fig no.13: Subjects required CPAP

Table no 10: Subjects on the basis of development of Necrotizing enterocolitis

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%Age	No. of cases	%Age			
NEC	NO	31	69%	29	64%	60	0.200	0.655
	YES	14	31%	16	36%	30		

90 neonates who were assessed in this study and as shown in above table no. 10, 30 neonates developed NEC, and the subjects who developed NEC were kept NPO (nil per oral) as per staging. Out of 30, 14 neonates who developed NEC were in group A while 16 were in group B.

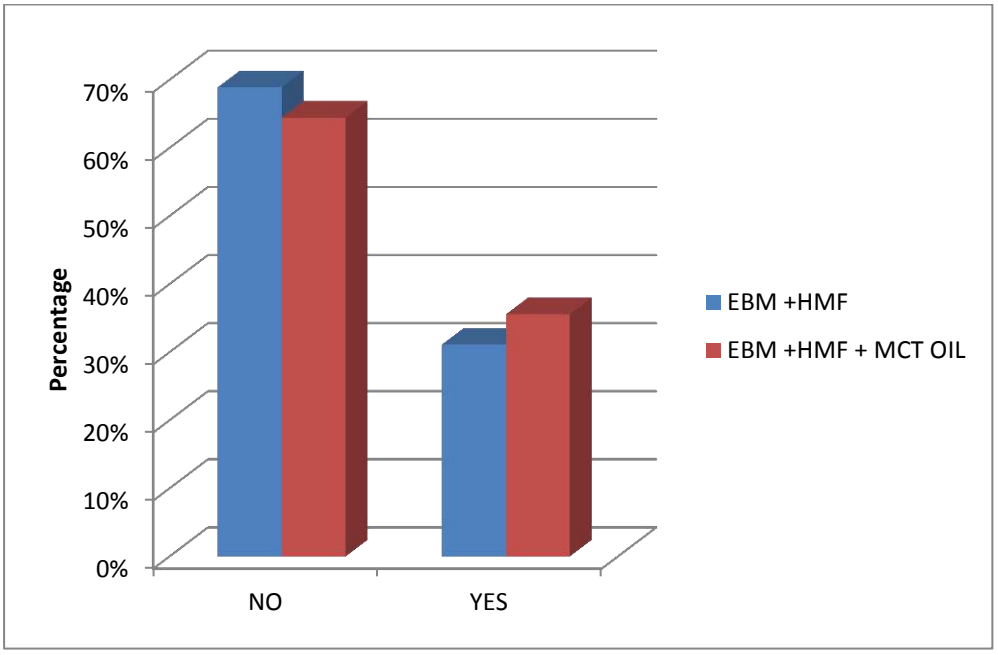


Fig no.14: Subjects having NEC

Table-11: Neonates received phototherapy

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%Age	No. of cases	%Age			
Need for phototherapy	NO	3	7%	11	24%	14	5.414	0.039
	YES	42	93%	34	76%	76		

As shown in table no11, Out of 90 neonates, 76 had hyperbilirubinemia for which they were given phototherapy. Out of 76, 34(76%) in group B who received phototherapy and 42(93%) were in group A and 14 neonates do not developed hyperbilirubinemia thus not requiring phototherapy with chisquare-5.414 and p value <0.05 (p=0.039)

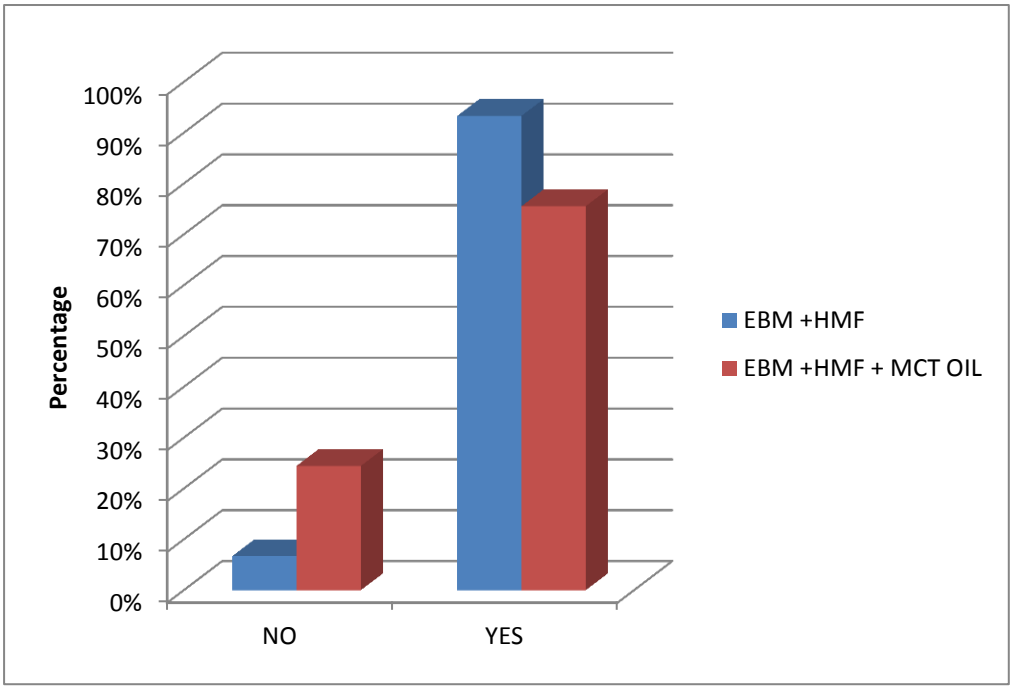


Fig no.15: Neonates received phototherapy

Table-12: Neonates received Exchange transfusion

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age			
Need for exchange transfusion	NO	43	96%	45	100%	88	2.045	0.153
	YES	2	4%	0	0%	2		

As shown in table no.12, out of 90 neonates, only 2 neonates had a range of hyperbilirubinemia on which exchange transfusion was performed. Rest 88 did not require it. Out of 88, 43 (96%) of group A and 45(100%) of group B do not require blood exchange transfusion. No statistically significance seen

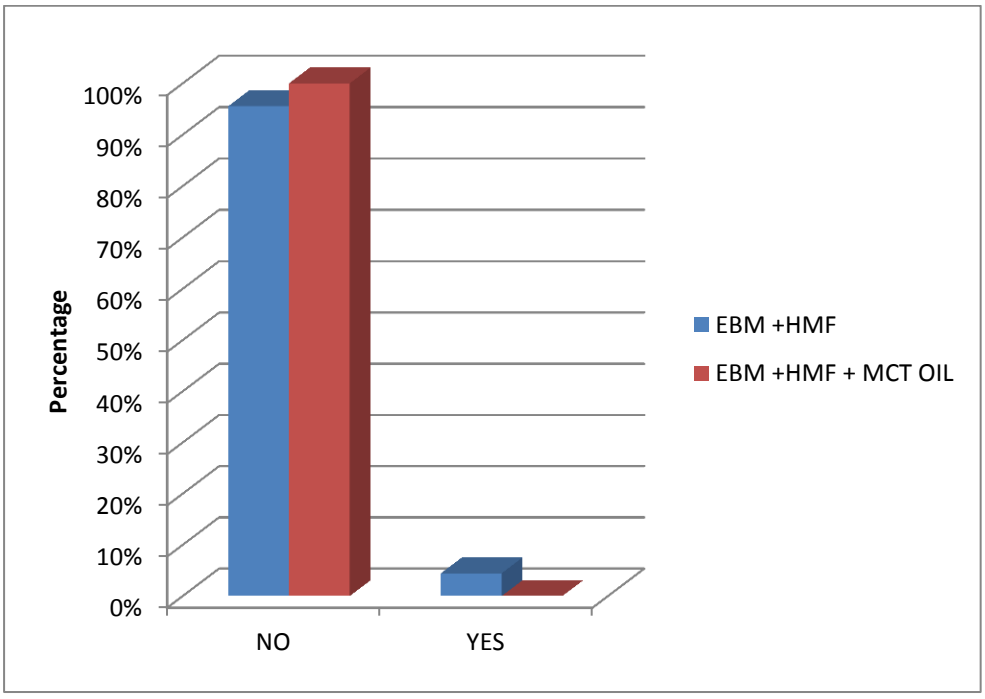


Fig no.16: Neonates received Exchange transfusion

Table no 13. Distribution of subjects on basis of birth weight

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age			
Birth weight group	< 1kg	9	20%	11	24%	20	0.257	0.612
	> 1kg	36	80%	34	76%	70		

As shown in table no13, out of 90 neonates, 20 neonates were with birth weight less than 1 kg and 70 neonates who weigh more than 1 kg. As per the data, 9 out of 20 were in group A (EBM+HMF) and 11 were in group B (EBM+HMF+MCT oil) whereas 36 out of 70 in group A and 34 in group B.

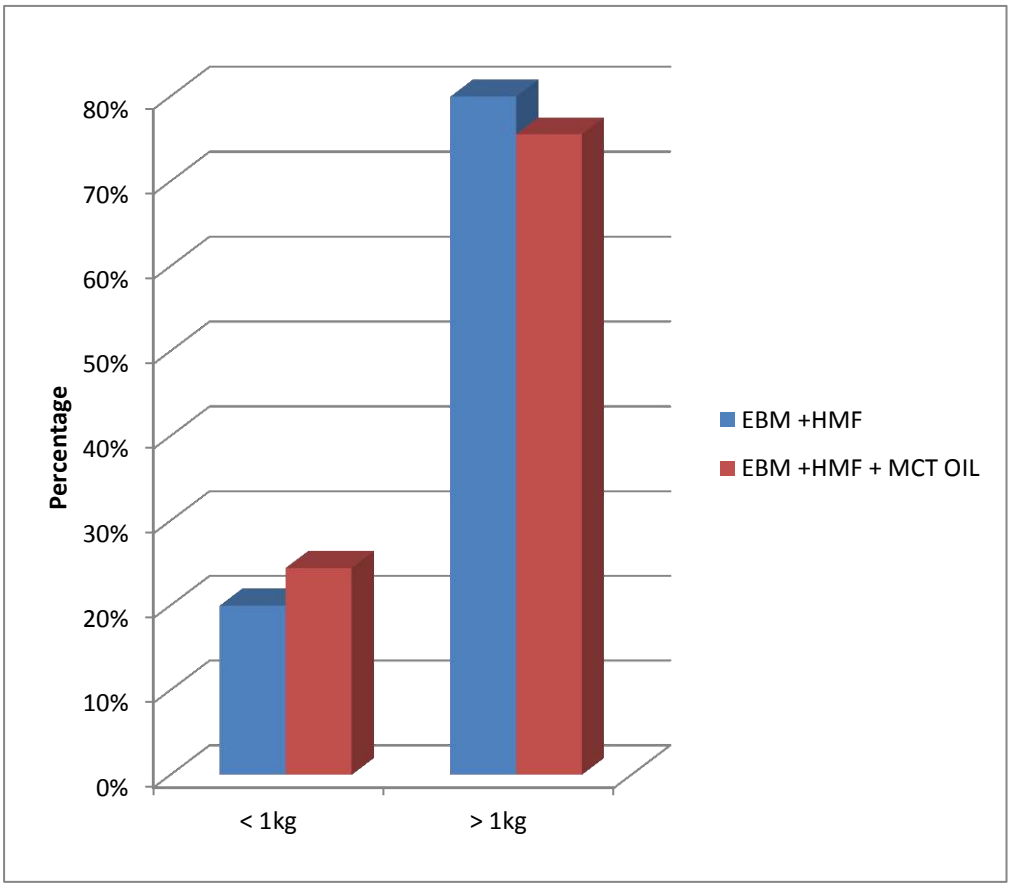


Fig no. 17: Birth weight group

Table-14: Neonates with abdominal distension

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%Age	No. of cases	%Age			
Increased	NO	41	91%	37	82%	78	1.538	0.215
	YES	4	9%	8	18%	12		

Abdominal distension is an important indicator of feed intolerance in VLBW neonates. Decision regarding when to stop feed, maintain or increase enteral feeding based on each neonate feeding intolerance. As shown in table no 14, out of total 90 neonates, total 12 had shown increase in abdominal girth while on feeds and out of 12,4(9%) were in group A while 8(18%) were in group B. rest 78 did not show the signs of abdominal distension suggesting they were tolerating feeds well.

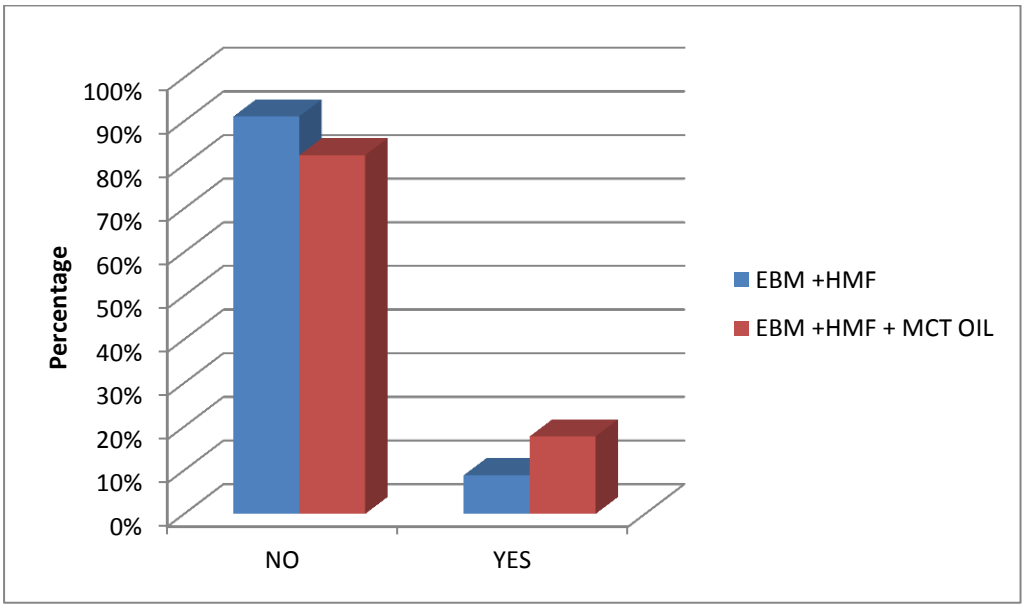


Fig no 18: Neonates developed abdominal distension during study period

Table no 15: Duration of NICU stay

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%Age	No. of cases	%Age			
NICU Stay (days) Decreased	NO	45	100%	44	98%	89	1.011	0.315
	YES	0	0%	1	2%	1		

Duration of NICU stay is important determinant in prognosis of neonate. As shown above (Table 15), only 2% of total neonates had shown decrease in duration of NICU stay, depicting that there is no additional benefit of MCT oil given along HMF in EBM per feed. (P=0.315)

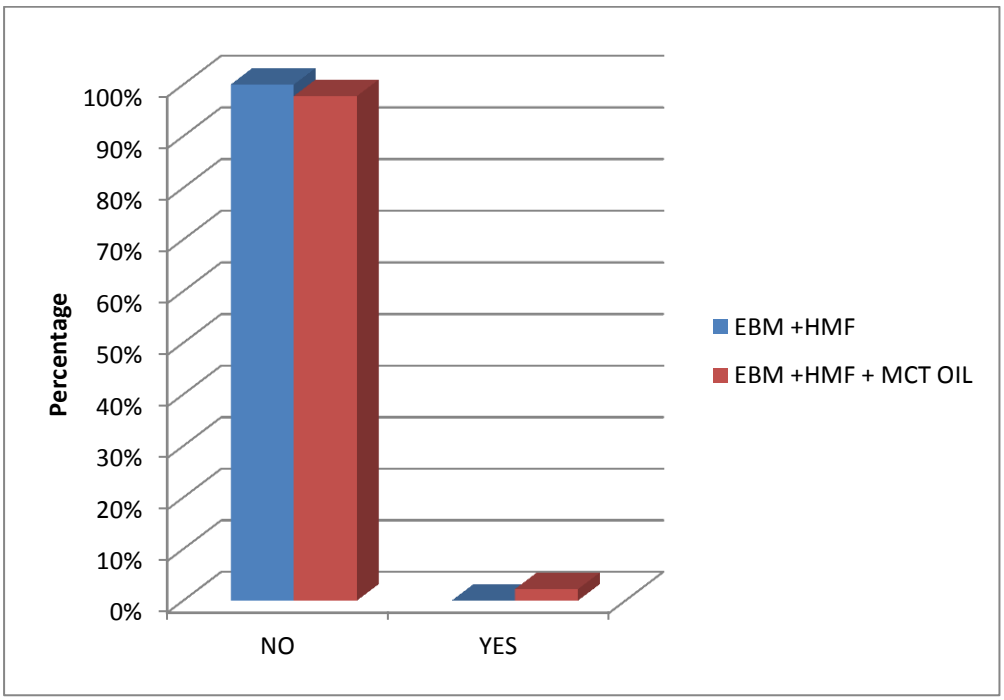


Fig no. 19: Duration of NICU stay

Table-16 Comparable weight gain/loss between two groups

		EBM +HMF		BM +HMF + MCT OIL		Total
		No. of cases	%age	No. of cases	%age	
Weight gain/loss	gain	45	100%	45	100%	90
Total		45	100%	45	100%	90

Table no 16, depicts that there was definite weight gain with addition of fortifiers. HMF was common in both the groups. But no major difference was seen in weight gain with addition of MCT oil along with HMF (group B). The weight gain in both the groups was similar.

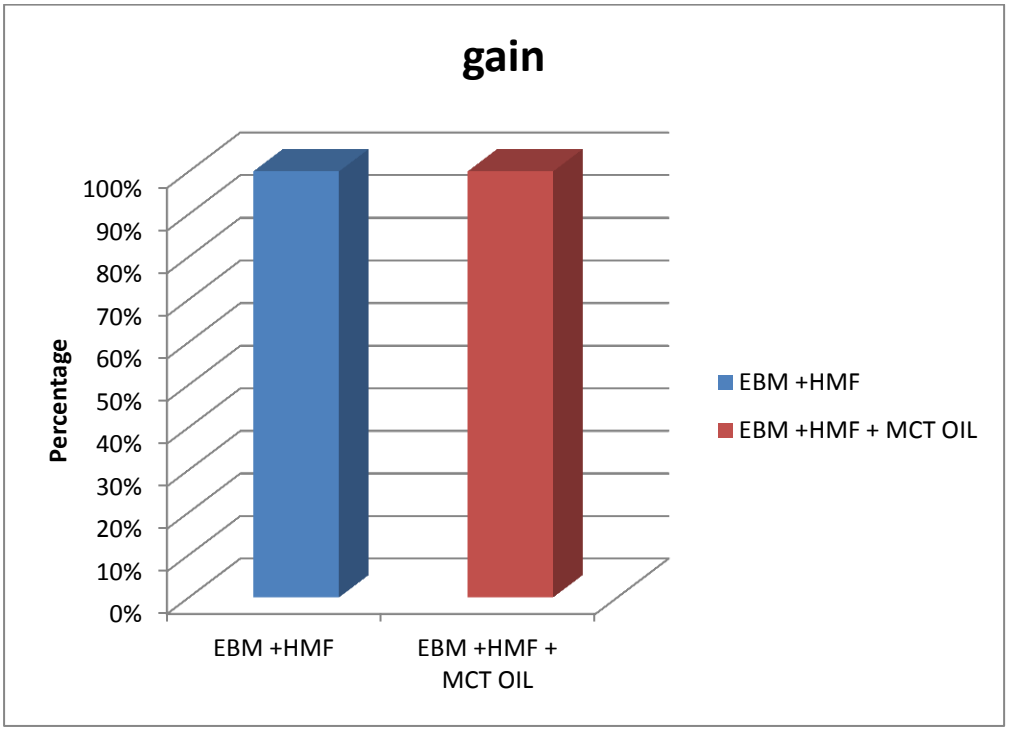


Fig no. 20: Comparable weight gain/loss between two groups

PRIMARY OUTCOME

Table-17: The comparison of weight gain between the neonates

	EBM +HMF		EBM +HMF + MCT OIL		t	p-value
	Mean	SD	Mean	SD		
Current Weight(gm) 1	1831.33	293	1900.22	310	1.139	0.258
percentage of gain/loss	13.5	5.39	14.3	5.84	0.619	0.538
Current Weight 2	2693.22	510.54	2858.11	407.09	-1.694	0.094
percentage %	14.17	4.87	15.04	3.32	-2.025	0.090

The primary outcome was to assess the weight gain. As shown in table no 17, there was definitive weight gain with addition of fortifiers with the mean percentage of weight gain during hospital stay was 13.5% with EBM +HMF, whereas the gain seen with EBM+HMF+MCT oil was 14.3% (p value= 0.538)

The mean gain after follow up was 14.17% with EBM +HMF, whereas the gain seen with EBM+HMF+MCT oil was 15.04% (p value 0.090). There was slightly better weight gain in group B than group A and both the groups were comparable for weight gain but none of them showing p<0.05.

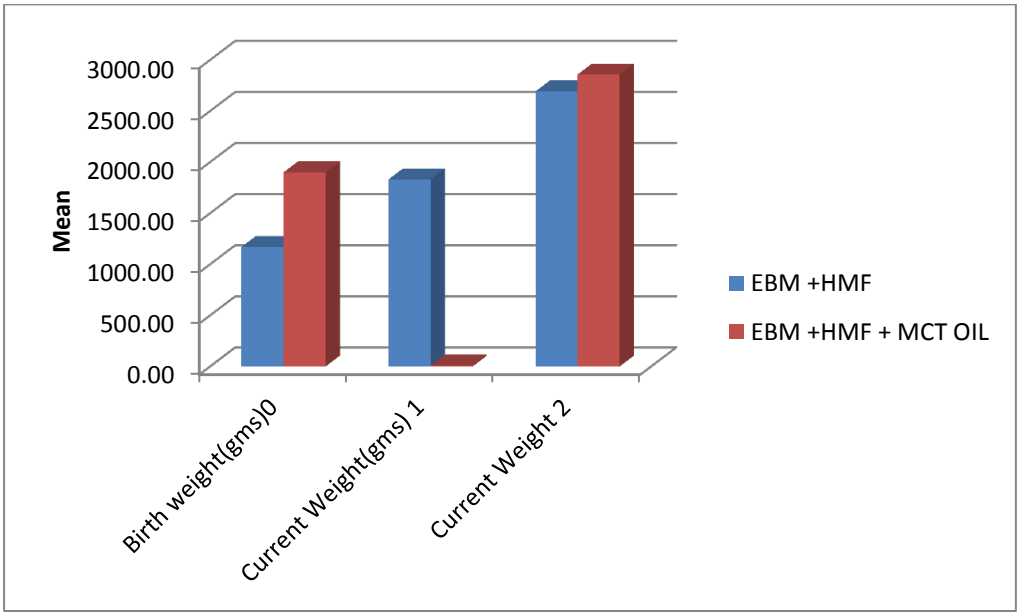


Fig no. 21: weight gain during and after hospital stay

SECONDARY OUTCOMES

Table-18 Duration of hospital stay

	EBM +HMF		EBM +HMF + MCT OIL		t	p-value
	Mean	SD	Mean	SD		
Duration of hospital stay(days)	33.84	15.84	33.62	18.33	0.062	0.951

The mean duration of neonates with EBM+HMF was 33.84 days whereas 33.62 with EBM+HMF+MCT oil, as shown in table no.18. It depicts that neonate who were in group B has slightly better outcome and lesser duration of stay in hospital and both the groups were comparable but were not statistically significant.

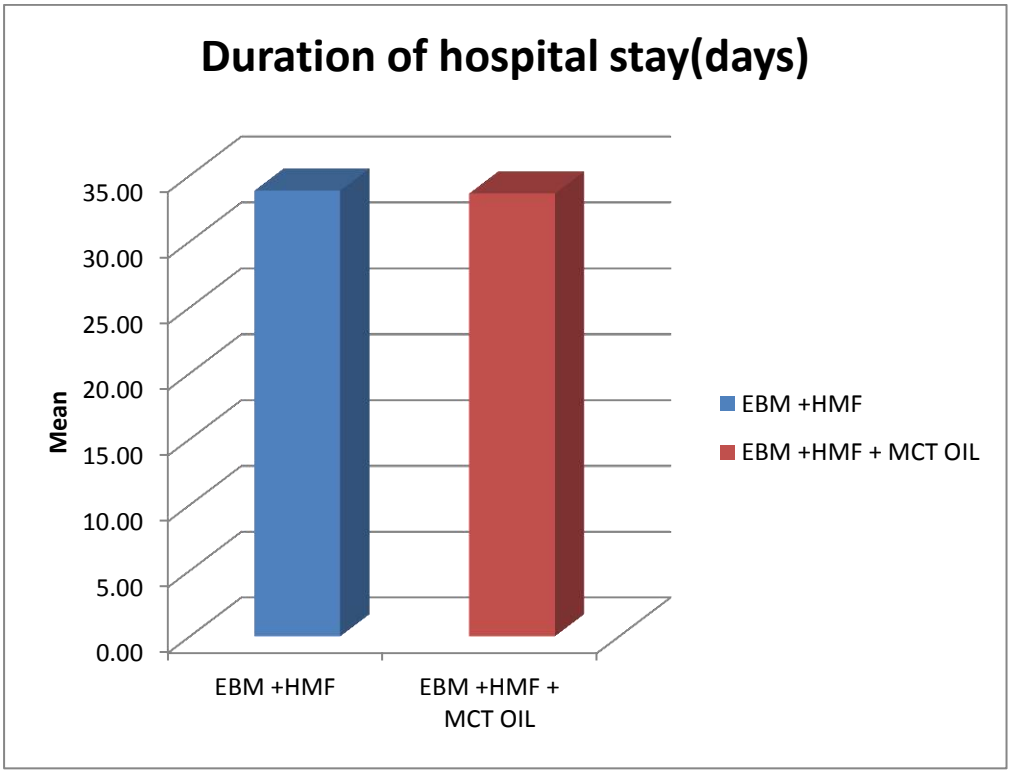


Fig no.22: Duration of hospital stay

Table no.19 Subjects with ROP

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		EBM +HMF	EBM +HMF	EBM +HMF + MCT OIL	EBM +HMF + MCT OIL			
ROP	ADVANCE	0	0%	1	2%	1	1.106	0.575
	EARLY	10	22%	11	24%	21		
	N	35	78%	33	73%	68		

The other outcomes such as Retinopathy of prematurity was also assessed and as shown in table no. 19, it was observed that total 22 out of 90 neonates had ROP and only 1 neonate out of 22 required treatments. Rest 68 did not develop retinopathy. 22% in group A and 24% in group B had retinopathy and 2% of group B had retinopathy that required treatment.

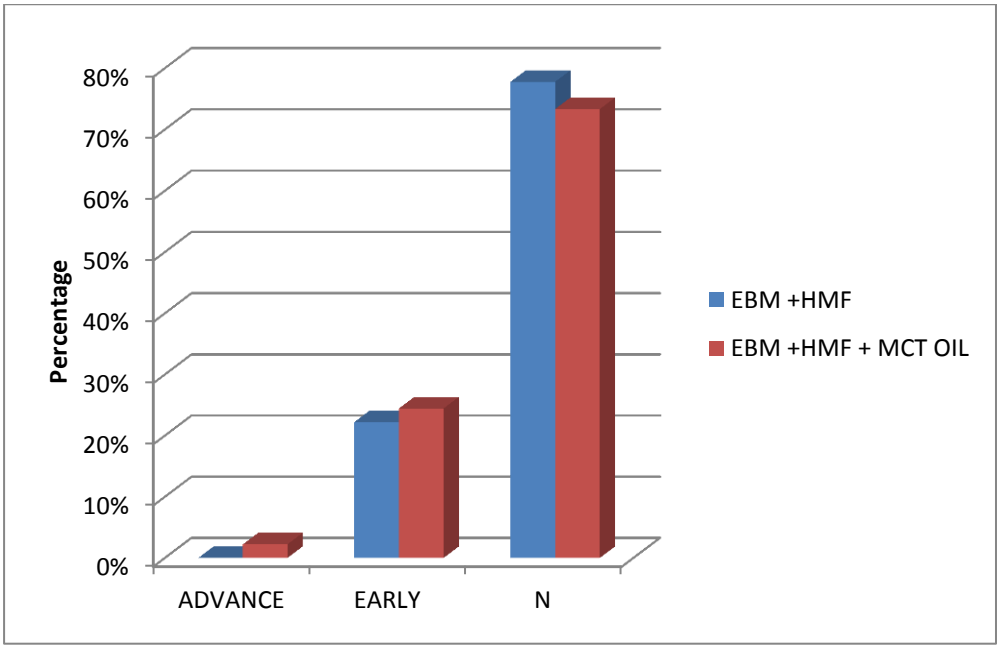


Fig no.23: Incidences of ROP

Table-20 Subjects with BPD

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%Age	No. of cases	%Age			
BPD	N	32	71%	37	82%	69	1.553	0.213
	Y	13	29%	8	18%	21		

Bronchopulmonary dysplasia (BPD) is one of the most important sequelae of premature birth. The concern is that lung injuries in early life might lead to lifelong consequences. As table 20, 90 neonates were analysed and was observed that 21 out of 90 neonates had BPD. 13 (29%) neonates from group A and 8(18%) were from group B. Total group analysis showed both the groups were comparable but not statistically significant (p value= 0.213)

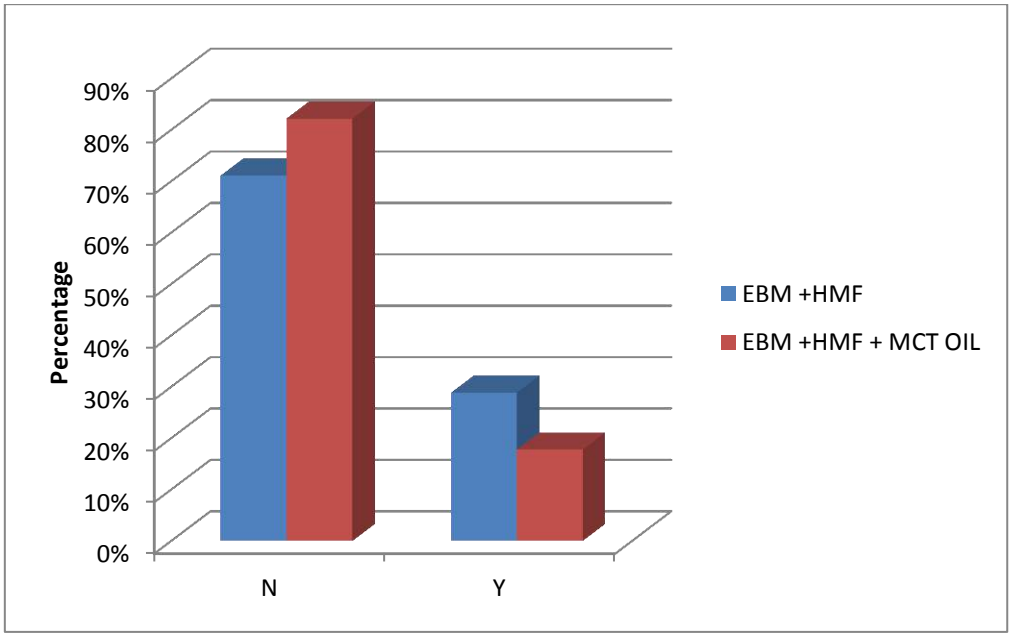


Fig no.24: Incidence of BPD in subjects during study period

Table-21 Subject with IVH

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		EBM +HMF	EBM +HMF	EBM +HMF + MCT OIL	EBM +HMF + MCT OIL			
IVH	N	44	98%	38	84%	82	4.939	0.058
	Y	1	2%	7	16%	8		

Intraventricular hemorrhage is a severe complication in VLBW neonates. The diagnosis of IVH was based on Ultrasound scan studies. Our subjects were screened and as shown in table no.21, 8 neonates had IVH out of 90 neonates. 1(2%) in group A and 7(16%) in group B had IVH. Both the groups were comparable and there was no statistically significant.

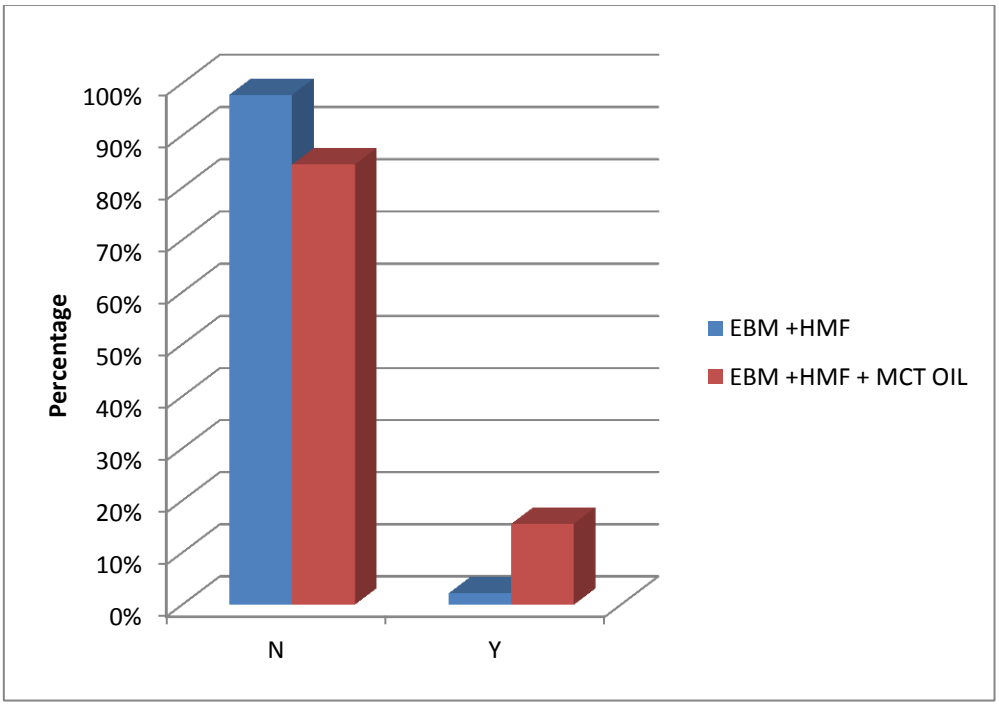


Fig no.25: IVH in subjects during study period

Table-22 Subjects with NEC

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age			
NEC	NO	31	69%	29	64%	60	0.200	0.655
	YES	16	36%	14	31%	30		

As shown in table no.22, Incidence of NEC (Necrotizing enterocolitis) was slightly higher in group A (36%) than group B (31%), and both the groups were comparable but not statistically significant (p value= 0.655)

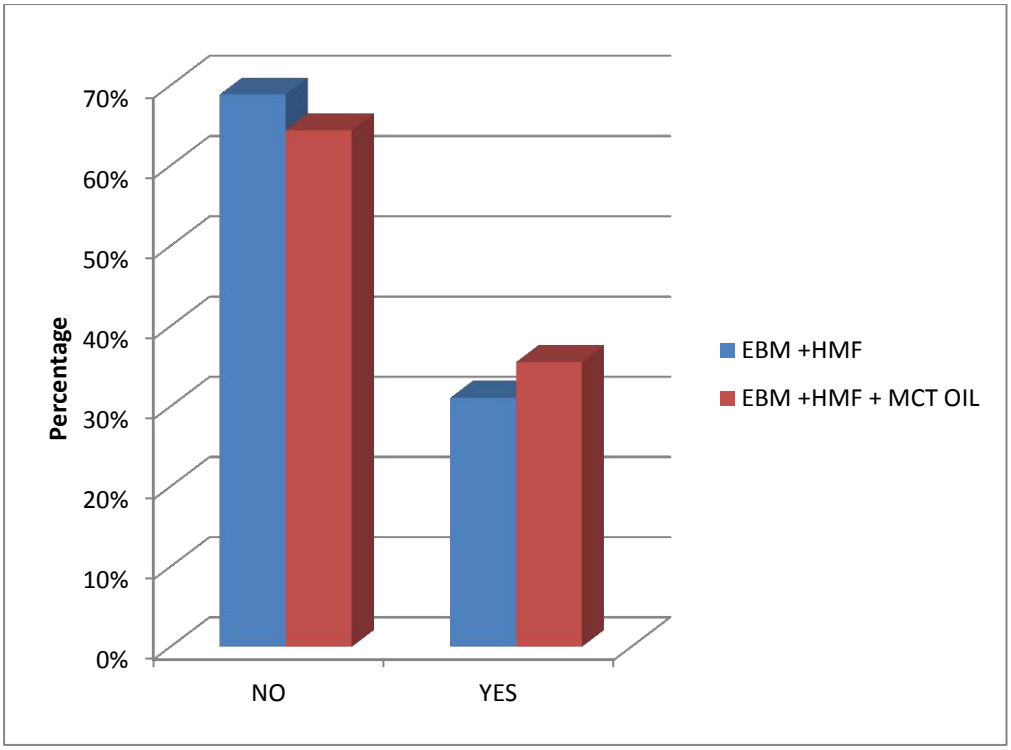


Fig no.26: Subjects with NEC

Table-23 Neonates having sepsis during hospital stay

		EBM +HMF		EBM +HMF + MCT OIL		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age			
Sepsis	NO	27	60%	23	51%	50	0.720	0.395
	YES	18	40%	22	49%	40		

Other morbidities of this study were sepsis, out of 90 neonates, 40 were positive for sepsis. Septic markers like c-reactive protein or procalcitonin were screened and levels were monitored serially. In the table no. 23, Both the groups were comparable and P value found to be > 0.05 which shows that on statistical analysis, these differences were not significant.

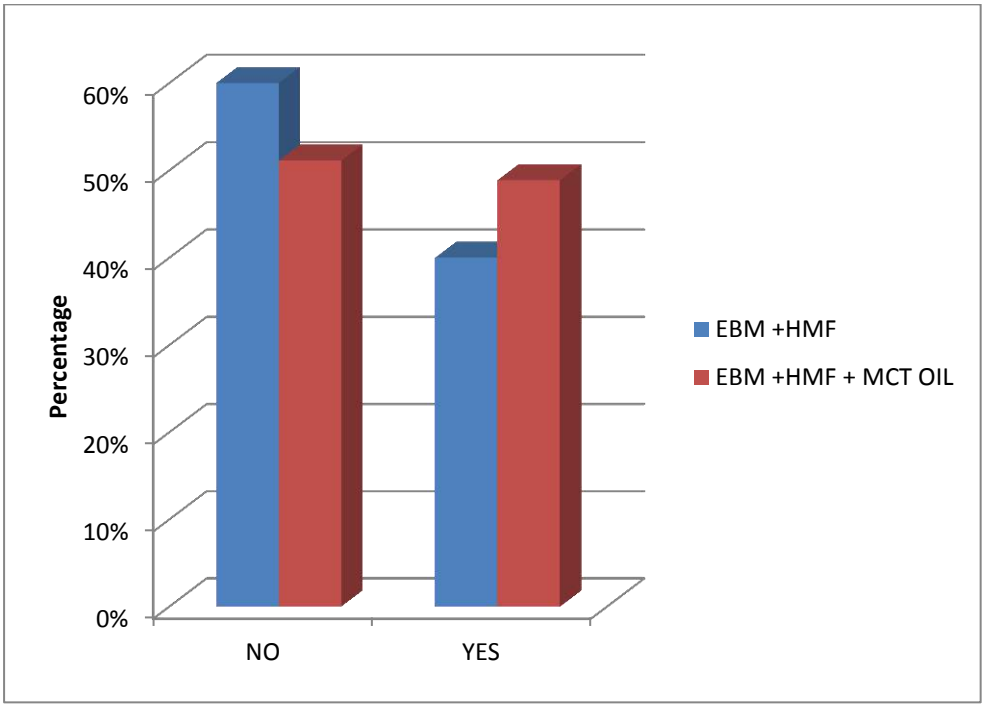


Fig no.27 Neonates having sepsis during hospital stay

DISCUSSION

This randomized controlled trial was carried out over a period of 1 year and 9 months from January 2019 to September 2020 in the department of Pediatrics of DMCH, Ludhiana, India. In this study, a total of 90 neonates were analyzed. The primary purpose of the study was to compare the weight gain in VLBW neonates when they were provided EBM + HMF vs EBM + HMF + MCT oil. Human milk offers many advantages and should be a default diet for all the neonates especially VLBW. The nutritional requirement of VLBW (< 1500g) neonates differ significantly from those with birth weight of 1500-2500gm because these VLBW neonates have low reserves. Despite potential benefits, human milk fails to meet the nutritive requirements of the VLBW neonates. Advancement in health care services has decreased the mortality rate of these compromised neonates but there is still increased morbidity due to prematurity, low immunity, low body reserves and extrauterine growth restriction (EUGR).[27] The nutritive content of human milk provides insufficient quantities of protein, calcium, sodium, phosphate to meet the estimated demands of neonates.[47] Physicians are facing challenges in providing proper nourishment to these neonates. To overcome this, human milk is fortified with commercially available fortifiers and it is seen that these available fortifiers helped in increasing weight gain and early discharge from NICU.

This study was conducted to analyze the effect of fortifiers, i.e. HMF + EBM vs HMF + EBM + MCT oil on these neonates. This study assessed the postnatal growth pattern of VLBW neonates and it was found that the use of fortification definitely leads to increase in weight gain and early discharge from NICU. However, there has been no study comparing only two groups using HMF and combination of both HMF +MCT OIL in EBM to see any improvement in weight gain. Therefore, the purpose of this study was to evaluate the clinical impact of modified nutrition protocol on the postnatal growth in VLBW neonates. Various studies in the literature assess the pattern of weight

gain with the use of fortifiers, keeping that in mind all VLBW neonates in this study were given fortified feeds and we did not take a control group of unfortified human milk.

Previous studies had discussed separately about the beneficial effects of HMF and MCT oil. Study by Martin EC et al [29], conducted a prospective double blinded randomized control trial on 40 neonates weighing less than 1500 gm and gestation period of less than 34 weeks and observed the weight gain and frequency of clinical complications in VLBW neonates until they reached 1800gm. Neonates were randomized into two groups: control (human milk) and intervention (fortified human milk). Fortifiers were added to manually expressed breast milk when feeding volume reached 100 mL/kg/day until newborns reached 1,800 g. Weight gain was monitored daily, They noticed that there was weight gain of 24.4 g/day in intervention group until reaching 1,800 g, compared to 21.1 g/day of the control group. This difference was statistically insignificant with p value being 0.075. In our study, we found that mean weight gain of VLBW babies who received HMF alone with EBM was 13.5g/day during their hospital stay. Complications found in their study between control and intervention groups were, digestive intolerance, 28 and 18%; abdominal distension, 10 and 20%; sepsis episodes, 25 and 20% respectively while in our study, feed intolerance was present in 53%, abdominal distension in 9% and sepsis episodes in 40% in the group receiving HMF + EBM.

Medium chain triglyceride oil found to be the major source of energy in VLBW neonates and the increase in weight gain was comparably more as per energy intake. It is great source of energy for neonates who need fluid restrictions. Before our study, there has been several studies on usefulness of MCT oil. In present study, we added MCT oil along HMF to determine its effect on weight gain. Study by Yamada T et al (23) demonstrated the effect of use of MCT oil and observed that neonates who were given MCT oil gained body weight better than the

control group (unfortified human milk) even though some of neonates were on restricted feed volumes (Neonates with PDA and BPD) The mean body weight gain was 19.7± 9.9 g/day in intervention group and was 19.7±9.9 g/day in control group and difference between the two groups was statistically insignificant. In contrast to present study where we have added MCT with HMF in expressed human milk (Group B) shown that the mean weight gain was 1900.22± 310 gm during hospital stays and 2858.11 ± 407 gm after 3 months follow up in high-risk clinic.

MCT oil was added to breast milk to enhance the calorie content and for better weight gain. In our unit, we have used MCT oil with HMF in EBM and it was administered in each feed. Study by Vaidya et al [41] assessed weight gain of 46 VLBW neonates with oral MCT oil (using coconut oil) and 22 were taken as control. They demonstrated a mean weight gain of 19.47±8.67 g/day increase in weight with MCT oil (p value <0.05). In our study, the weight gain in group B was 14.3 ± 5.84 g/day. The present demonstrated that there was no statistically significant increase in weight gain after supplementation of expressed breast milk with oral MCT oil along with HMF.

Study by Thureen et al. [48] demonstrated that the incidence of postnatal growth retardation was less when VLBW neonates were supplied with 3 g/kg/day of protein from the first day. In addition, Dit Trolli et al [49] reported that there was better outcome in neurological development and weight gain with addition of lipids for neonates less than 28 weeks in the first 14 days. Based on these studies, it recommends that supply of lipids and proteins should be started from first day of birth and increased gradually.[50] In contrast to our study, we have used standardized fortification in form of Lactodex human milk fortifiers and simyl MCT oil in standard doses and supplied lipids in form of MCT oil only and that was started when study subjects reached to feed volume @ 100 ml/kg/day.

IVH (Intraventricular haemorrhage) is also a major debatable problem of VLBW neonates. The stay of hospital could be increased with the presence of IVH. In the present study, the incidence of IVH was 2 % in group A (EBM + HMF) and 16% in group B (EBM+HMF+MCT oil) but the difference was not statistically significant. Again, there is no such study to compare the incidence of IVH and duration of hospital stay with use of fortifiers.

Only comparable study to this present study was done by Joshi et al[17], who did a prospective cohort study comprising of 225 VLBW neonates divided into 3 groups of 75 neonates each receiving EBM + HMF in group 1, EBM + HMF + MCT oil in group 2 and EBM + HMF + Coconut oil in group 3 and observed that the difference in weight gain among the 3 groups was statistically insignificant at the endpoint and the results were similar to the present study.

Nutrition plays a major role in the prevention as well as in management of neonates with BPD, and a vicious cycle may occur. In BPD growth failure is predominantly due to malnutrition. As malnutrition compromised lung development and function.[51] Several studies found that those who were given nutritional supplementation had less incidence of BPD as compared to those who were not. One study by Klevebro et al.[52] on 296 extremely preterm neonates and found that the incidence of BPD and ROP were significantly reduced by giving more nutrition. The study found that energy intake in combination with protein intake had a positive impact on weight gain and every additional 10 kcal/kg/day in energy intake was associated with a 9% reduction in the risk of BPD. The present study is the first study so far comparing the incidences of BPD and ROP on addition of HMF vs HMF+ Mct oil to EBM and found that the results were comparable, though the incidences were less in group B (EBM+HMF+MCT oil) as compared to group A. (EBM+HMF)

The aim of our study was to analyse the weight gain with usage of HMF with EBM vs EBM + HMF + MCT. The secondary objective was to analyse the length of hospital stay and short-term outcomes such as BPD, ROP, IVH, sepsis. Short term growth is difficult to assess particularly in initial weeks of life when weight loss is common. VLBW neonates mostly have long hospital stay, a small benefit in weight gain might have significant impact on growth parameters at discharge.

A total of 90 VLBW neonates randomized into two groups and were analysed for differences in weight gain, length of hospital stays, oxygen dependency, need of CPAP, incidences of BPD, ROP, IVH, sepsis. The difference in these variables between the two groups was statistically insignificant. Although the neonates in group 2 (EBM+HMF+MCT) showed better mean weight gain, However the result was not statistically significant. There was lesser hospital stay and need of CPAP, the incidence of BPD was less in group B comparably although the results were not statistically significant. The incidence of ROP was less in group A but the difference between them was statistically insignificant. Fortification of human milk appeared to have beneficial effect on nutrition and growth of the neonates studied over short period of time. Comparably with other studies, this present study suggests that the addition of MCT oil does not provide much difference

There were limitations to our study. It was a non-blinded randomised control trial with small sample size. We could not demonstrate long term benefits which may be better concluded with multicentric, blinded, randomized control trial with large sample size that get better results.

SUMMARY & CONCLUSION

- This study was conducted to analyze the effect of fortifiers, i.e. HMF + EBM vs HMF + EBM + MCT oil on these neonates. The postnatal growth pattern of VLBW neonates was assessed and result showed that there was definite weight gain in each group and addition also helped in early discharge from NICU.
- In summary, fortified human milk has tremendous benefits in improving the growth and short-term outcomes of premature neonates. Human milk has clear advantage advantages due to its composition. VLBW neonates need fortification of human milk to achieve weight gain. Based on the results of this study, we concluded that the addition of MCT oil to EBM along HMF has no additional benefit in weight gain
- Even though further studies with more sample size and longer follow up will gives us better results.

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S.No.	Name	MRD No	DOB	DOA	DOD	Duration of hospital stay(days)	Gender	Gestation (weeks)	Gestation (weeks) group	GROWTH STATUS	Mode of Delivary	Birth weight in Grams	APGAR Scores (for inborn) at 1min	APGAR Scores at 5 min	REASON FOR ADMISSION_Prematurity	Respiratory symptom	Respiratory failure	Sepsis evaluation	Peri natal Asphyxia	Seizures	Hypoglycemia	Hyper Bilirubinemia
1	B/O K	909410	02-03-2020	02-03-2020	06-04-2020	35	male	32	2	SGA	LSCS	990	5	8	YES	YES	YES	NO	NO	NO	NO	NO
2	b/o M	905631	25-02-2020	25-02-2020	31-03-2020	36	female	28	1	AGA	LSCS	1090	7	9	YES	YES	YES	YES	NO	NO	NO	NO
3	B/o R	885204	22-01-2020	22-01-2020	08-04-2020	77	Male	26	1	AGA	NVD	800	-	-	YES	YES	YES	NO	NO	NO	NO	YES
4	B/o T	900477	17-02-2020	17-02-2020	21-03-2020	34	female	29	1	SGA	LSCS	940	7	9	YES	YES	NO	NO	NO	NO	NO	NO
5	B/o J	922051	12-04-2020	12-04-2020	04-05-2020	22	female	30	2	AGA	LSCS	1490	7	9	YES	YES	NO	NO	NO	NO	NO	NO
6	B/o M twin 1	932492	06-06-2020	06-06-2020	02-07-2020	52	female	29	1	AGA	LSCS	1200	7	8	YES	YES	NO	YES	NO	NO	NO	NO
7	B/o P	928481	22-05-2002	22-05-2020	06-08-2020	69	Male	25	1	AGA	NVD	805	6	7	NO	YES	YES	NO	YES	NO	NO	NO
8	B/o S twin-1	947059	25-07-2020	25-07-2020	09-09-2020	17	male	28	1	AGA	LSCS	1160	7	8	YES	YES	NO	NO	YES	NO	NO	NO
9	B/o S twin-2	956832	19-08-2020	19-08-2020	18-09-2020	31	male	30	2	AGA	LSCS	1060	7	8	YES	YES	NO	NO	NO	NO	NO	NO
10	B/o R	958653	24-08-2020	24-08-2020	11-09-2020	18	male	31	2	AGA	LSCS	1300	5	8	YES	YES	NO	NO	NO	NO	NO	NO
11	B/o S	959479	26-08-2020	26-08-2020	22-09-2020	26	female	30	2	AGA	NVD	1200	5	8	YES	YES	NO	NO	YES	NO	NO	NO
12	B/o A	960689	30-08-2020	30-08-2020	12-09-2020	13	male	31	2	AGA	LSCS	1490	5	7	YES	YES	NO	NO	NO	NO	NO	NO
13	B/o P twin-2	960353	28-08-2020	28-08-2020	23-09-2020	26	male	31	2	AGA	LSCS	1280	5	7	YES	YES	NO	NO	NO	NO	NO	NO
14	B/o S	960009	28-08-2020	28-08-2020	11-09-2020	14	female	34	2	SGA	LSCS	1000	6	9	YES	YES	NO	YES	NO	NO	NO	NO
15	B/o S	965826	15-09-2020	15-09-2020	04-10-2020	19	male	31	2	SGA	LSCS	1145	6	8	YES	YES	NO	YES	NO	NO	NO	NO
16	B/o M	965099	12-09-2020	12-09-2020	02-10-2020	20	female	31	2	AGA	LSCS	1330	7	8	YES	YES	NO	NO	NO	NO	NO	NO
17	B/o H twin-2	963729	08-09-2020	08-09-2020	05-10-2020	28	female	32	2	SGA	LSCS	1175	8	9	YES	YES	NO	YES	NO	NO	NO	NO
18	B/o H twin-1	963728	08-09-2020	08-09-2020	07-10-2020	30	male	32	2	SGA	LSCS	1200	8	9	YES	YES	NO	YES	NO	NO	NO	NO
19	B/o J	977277	18-10-2020	18-10-2020	30-10-2020	13	female	31	2	AGA	LSCS	1465	6	8	YES	YES	NO	NO	YES	NO	NO	NO
20	B/o R	976765	16-10-2020	16-10-2020	18-11-2020	32	female	32	2	SGA	LSCS	1060	7	9	YES	YES	NO	NO	NO	NO	NO	NO
21	b/o H	977623	19-10-2020	19-10-2020	29-11-2020	40	Male	29	1	AGA	LSCS	940	9	10	YES	YES	NO	NO	NO	NO	NO	NO
22	B/o K	988532	18-11-2020	18-11-2020	16-12-2020	28	Female	30	2	AGA	LSCS	1340	8	9	YES	YES	NO	NO	NO	NO	NO	NO
23	B/o S	983996	06-11-2020	06-11-2020	30-12-2020	55	female	28	1	AGA	LSCS	1020	7	8	YES	YES	NO	NO	NO	NO	NO	NO
24	B/o S	983488	04-11-2020	04-11-2020	21-12-2020	48	female	28	1	AGA	LSCS	865	6	7	YES	YES	NO	NO	NO	NO	NO	NO
25	B/o R twin-1	988299	17-11-2020	17-11-2020	29-12-2000	42	female	31	2	SGA	LSCS	885	8	9	YES	YES	NO	NO	NO	NO	NO	NO
26	B/o D	989244	19-11-2020	19-11-2020	12-12-2020	24	female	31	2	AGA	LSCS	1370	7	9	YES	YES	NO	NO	NO	NO	NO	NO
27	B/o S	989684	20-11-2020	20-11-2020	13-01-2020	55	male	26	1	AGA	NVD	840	5	8	YES	YES	YES	NO	YES	NO	NO	NO
28	B/o R twin-2	988300	17-11-2020	17-11-2020	13-01-2021	58	male	30	2	SGA	NVD	785	8	9	YES	YES	NO	NO	NO	NO	NO	NO
29	B/o G	997162	08-12-2020	08-12-2020	20-12-2020	12	male	35	2	SGA	LSCS	1420	6	8	YES	YES	YES	YES	YES	NO	NO	NO
30	B/o N	993334	29-11-2020	29-11-2020	12-10-2021	45	male	28	1	AGA	LSCS	1200	nk	-	YES	YES	YES	YES	NO	NO	YES	NO
31	B/o H	1004900	25-12-2020	25-12-2020	20-01-2020	27	male	31	2	SGA	LSCS	1040	8	9	YES	YES	NO	NO	NO	NO	NO	NO
32	B/o S	924901	04-05-2020	04-05-2020	01-06-2020	27	female	32	2	SGA	LSCS	980	8	9	YES	YES	NO	YES	NO	NO	NO	NO
33	B/O G twin-1	1001516	17-12-2020	17-12-2020	25-01-2021	40	male	30	2	AGA	LSCS	1380	6	8	YES	YES	NO	NO	NO	NO	NO	NO
34	B/o R twin-2	985733	10-11-2020	10-11-2020	08-01-2021	60	male	25	1	AGA	LSCS	690	6	8	YES	YES	YES	YES	YES	NO	NO	NO
35	B/o R	1015276	20-01-2021	20-01-2021	10-02-2021	20	female	34	2	SGA	LSCS	1080	7	9	YES	YES	NO	NO	NO	NO	NO	NO
36	B/o G	1001517	17-12-2020	17-12-2020	25-01-2021	38	male	29	1	AGA	LSCS	1220	5	7	YES	YES	NO	YES	NO	NO	NO	NO
37	B/o A	9262027	12-05-2020	12-05-2020	15-06-2020	35	male	28	1	AGA	LSCS	1090	7	9	YES	YES	NO	NO	NO	NO	NO	NO
38	B/o M	933774	11-06-2020	11-06-2020	16-06-2020	6	male	36	2	SGA	LSCS	1480	-	-	YES	YES	NO	NO	NO	NO	NO	NO
39	B/o U	936627	22-06-2020	22-06-2020	07-08-2020	46	male	29	1	SGA	LSCS	1080	5	7	YES	YES	YES	NO	YES	NO	NO	NO
40	B/O A	1001877	18-12-2020	18-12-2020	01-02-2021	46	Female	29	1	AGA	LSCS	1030	7	9	YES	YES	NO	NO	NO	NO	NO	NO
41	B/o M	999302	12-12-2020	12-12-2020	06-02-2021	57	male	27	1	AGA	LSCS	830	6	8	YES	YES	YES	NO	NO	NO	NO	NO
42	B/o P	1003240	22-12-2020	22-12-2020	13-02-2021	54	male	30	2	AGA	LSCS	1000	6	9	YES	YES	NO	NO	NO	NO	NO	NO
43	B/o A	943572	15-07-2020	15-07-2020	23-08-2020	43	male	28	1	AGA	LSCS	940	7	9	YES	YES	NO	NO	NO	NO	NO	NO
44	B/o N	902926	20-02-2020	20-02-2020	06-03-2020	16	female	32	2	SGA	LSCS	1420	7	9	YES	YES	NO	NO	NO	NO	NO	NO
45	B/o R	1014916	19-01-2021	20-01-2021	15-03-2021	55	male	28	1	AGA	NVD	1150	6	8	YES	YES	YES	NO	YES	NO	NO	NO
46	B/o G	1014058	18-01-2021	18-01-2021	22-02-2021	36	male	32	2	AGA	LSCS	1200	6	8	YES	YES	YES	NO	NO	NO	NO	NO
47	b/o D	1029419	17-02-2021	17-02-2021	13-03-2021	26	female	30	2	AGA	LSCS	1160	8	9	YES	YES	NO	NO	NO	NO	NO	NO
48	B/o R twin-1	1036246	28-02-2021	28-02-2021	16-03-2021	17	male	32	2	AGA	LSCS	1460	-	-	YES	YES	NO	NO	NO	NO	NO	NO
49	B/o M	1020325	31-01-2021	31-01-2021	13-03-2021	42	male	28	1	AGA	LSCS	1230	8	9	YES	YES	YES	NO	NO	NO	NO	NO
50	B/o r twin-2	1036248	28-02-2021	28-02-2021	16-03-2021	17	female	32	2	AGA	LSCS	1360	-	-	YES	YES	NO	NO	NO	NO	NO	NO
51	B/o Y twin-1	1050916	13-03-2021	13-03-2021	14-05-2021	62	male	27	1	AGA	LSCS	1120	7	9	YES	YES	YES	YES	YES	NO	NO	NO
52	B/o S twin-2	979543	24-10-2020	24-10-2020	25-11-2020	31	male	30	2	AGA	LSCS	1400	7	8	YES	YES	NO	NO	NO	NO	NO	NO
53	B/o Y twin-2	1050918	13-03-2021	13-03-2021	14-05-2021	61	male	27	1	AGA	LSCS	1130	7	9	YES	YES	YES	NO	NO	NO	NO	NO
54	B/o B	1123816	11-06-2021	17-06-2021	06-07-2021	19	male	31	2	AGA	LSCS	1460	-	-	YES	YES	YES	YES	NO	NO	NO	NO
55	B/o K	1101098	02-05-2021	02-05-2021	06-07-2021	66	male	28	1	AGA	LSCS	1080	7	8	YES	YES	NO	NO	NO	NO	NO	NO
56	B/o K	943690	15-07-2020	15-07-2020	07-08-2020	24	male	30	2	AGA	LSCS	1200	5	6	YES	YES	NO	NO	YES	NO	NO	NO

S.No.	Name	Metabolic evaluation	Small for gestational Age	Large for gestational age	Birth asphyxia requiring bag and mask evaluation	BPD	Need for ventilation	Duration of ventillatory support(days)	RDS	Need for surfactant	Apnea of pre maturity	Feed intolerance	Need for ionotropes	Need for CPAP	NEC	Need for phototherapy	Need for exchange transfusion	Abnormal ROP Screening	Findings	ROP
1	B/O K	NO	YES	NO	YES	Y	YES	3	YES	YES	NO	YES	NO	YES	YES	YES	NO	-	-	N
2	b/o M	NO	NO	NO	YES	Y	YES	7	YES	YES	NO	YES	NO	YES	YES	YES	NO	-	-	N
3	B/o R	YES	YES	NO	NO	Y	YES	14	YES	YES	YES	YES	YES	YES	NO	YES	NO	-	-	N
4	B/o T	NO	YES	NO	NO	N	NO	-	YES	NO	NO	NO	NO	YES	YES	YES	NO	43906	l/e zone 2 and right eye satge 1	EARLY
5	B/o J	NO	NO	NO	NO	N	NO	-	YES	NO	YES	YES	NO	YES	YES	YES	NO	-	-	N
6	B/o M twin 1	NO	NO	NO	NO	N	NO	-	YES	YES	YES	YES	NO	YES	YES	YES	NO	44032	zone 2 stage 1 , no prepluse disease	EARLY
7	B/o P	NO	NO	NO	YES	Y	YES	14	YES	YES	YES	NO	NO	YES	YES	YES	NO	44048	zone2 satge 3, mild prepluse disease	ADVANCE
8	B/o S twin-1	NO	NO	NO	YES	N	NO	-	YES	NO	NO	NO	NO	YES	NO	NO	NO	44082	zone 2 stage 2	EARLY
9	B/o S twin-2	NO	NO	NO	NO	N	NO	-	YES	NO	NO	NO	NO	YES	NO	YES	NO	44091	B/L ZONE 2 STAGE 2	EARLY
10	B/o R	NO	NO	NO	YES	N	NO	-	YES	NO	YES	NO	NO	YES	NO	YES	NO	-	-	N
11	B/o S	NO	NO	NO	YES	N	NO	-	YES	NO	YES	NO	NO	YES	NO	YES	NO	-	-	N
12	B/o A	NO	NO	NO	YES	N	NO	-	YES	NO	NO	NO	NO	YES	NO	YES	NO	-	-	N
13	B/o P twin-2	NO	NO	NO	YES	N	NO	-	YES	NO	NO	NO	NO	YES	NO	YES	NO	44091	zone 1,stage 1	EARLY
14	B/o S	NO	YES	NO	NO	N	NO	-	YES	NO	NO	NO	NO	YES	NO	YES	NO	-	-	N
15	B/o S	NO	NO	NO	NO	N	NO	-	YES	NO	YES	NO	NO	YES	NO	YES	NO	-	-	N
16	B/o M	NO	NO	NO	NO	N	NO	-	YES	NO	NO	YES	NO	YES	NO	NO	NO	-	-	N
17	B/o H twin-2	NO	YES	NO	NO	N	NO	-	YES	NO	NO	NO	NO	NO	YES	YES	NO	-	-	N
18	B/o H twin-1	NO	YES	NO	NO	N	NO	-	YES	NO	NO	YES	NO	YES	NO	YES	NO	-	-	N
19	B/o J	NO	NO	NO	YES	Y	YES	4	YES	YES	YES	NO	NO	YES	NO	YES	NO	-	-	N
20	B/o R	NO	YES	NO	NO	N	NO	-	YES	NO	NO	YES	NO	YES	YES	YES	NO	-	-	N
21	b/o H	NO	NO	NO	NO	N	NO	-	YES	YES	YES	YES	NO	YES	YES	YES	NO	44161	b/l zone 2 satge 2	EARLY
22	B/o K	NO	NO	NO	NO	N	NO	-	YES	NO	YES	NO	NO	NO	NO	NO	NO	44179	early AP ROPaterial tortuosity	EARLY
23	B/o S	NO	NO	NO	NO	N	NO	-	YES	NO	YES	YES	YES	YES	NO	YES	NO	43885	stage 2 , zone 2 r/e,l/e zone 2 early stage 1	EARLY
24	B/o S	NO	NO	NO	YES	Y	YES	6	YES	YES	YES	YES	YES	YES	YES	YES	NO	44175	zone 2 early stage 2	EARLY
25	B/o R twin-1	NO	YES	NO	NO	N	NO	-	YES	YES	NO	YES	NO	YES	YES	YES	NO	44182	zone 2 stage 2	EARLY
26	B/o D	NO	NO	NO	NO	N	NO	-	YES	NO	NO	YES	NO	YES	NO	YES	NO	-	-	N
27	B/o S	NO	NO	NO	YES	Y	YES	7	YES	YES	YES	NO	YES	YES	NO	YES	NO	-	-	N
28	B/o R twin-2	NO	YES	NO	NO	N	NO	-	YES	YES	YES	YES	NO	YES	YES	YES	NO	44203	zone 2 stage 1	EARLY
29	B/o G	NO	YES	NO	YES	N	NO	-	YES	YES	NO	NO	YES	YES	NO	NO	NO	-	-	N
30	B/o N	NO	NO	NO	NO	Y	YES	10	YES	NO	NO	NO	NO	YES	YES	NO	NO	43861	zone 2 satge 1	EARLY
31	B/o H	NO	YES	NO	NO	N	NO	-	YES	NO	NO	YES	NO	YES	NO	YES	NO	44240	zone 2 stage 1	EARLY
32	B/o S	NO	YES	NO	NO	N	NO	-	YES	NO	NO	NO	NO	YES	NO	YES	NO	-	-	N
33	B/O G twin-1	NO	NO	NO	NO	N	NO	-	YES	NO	YES	YES	NO	YES	NO	YES	NO	44232	ZONE2 STAGE2 (L>R)	EARLY
34	B/o R twin-2	NO	NO	NO	YES	Y	YES	7	YES	YES	NO	NO	NO	YES	NO	YES	NO	44203	zone 2 , stage 1, no prepluse disease	EARLY
35	B/o R	NO	YES	NO	NO	N	NO	-	YES	NO	YES	YES	NO	YES	NO	YES	NO	-	-	N
36	B/o G	NO	NO	NO	YES	Y	YES	5	YES	YES	YES	YES	YES	YES	NO	YES	NO	44232	zone 2 stage 2 , no prepluse disease	EARLY
37	B/o A	NO	NO	NO	NO	N	NO	-	YES	NO	YES	NO	NO	YES	NO	YES	NO	-	-	N
38	B/o M	NO	YES	NO	NO	N	NO	-	NO	NO	NO	YES	NO	NO	NO	YES	NO	-	-	N
39	B/o U	NO	NO	NO	YES	Y	YES	10	YES	YES	YES	NO	NO	YES	NO	YES	NO	44049	zone 2 stage 2 b/l	EARLY
40	B/O A	NO	NO	NO	NO	N	NO	-	YES	NO	YES	YES	NO	YES	NO	YES	NO	-	-	N
41	B/o M	NO	NO	NO	YES	Y	YES	4	YES	YES	YES	YES	NO	YES	NO	YES	NO	44233	B/L ZONE 2 STAGE 2	EARLY
42	B/o P	NO	NO	NO	YES	N	NO	-	YES	NO	YES	YES	NO	YES	YES	YES	NO	-	-	N
43	B/o A	NO	NO	NO	NO	N	NO	-	YES	YES	YES	NO	NO	YES	NO	YES	NO	-	-	N
44	B/o N	NO	YES	NO	NO	N	NO	-	YES	NO	YES	YES	NO	YES	NO	YES	NO	-	-	N
45	B/o R	NO	NO	NO	YES	Y	YES	7	YES	YES	YES	NO	NO	YES	NO	YES	NO	-	-	N
46	B/o G	NO	NO	NO	YES	Y	YES	2	YES	YES	YES	YES	NO	YES	NO	YES	NO	-	-	N
47	b/o D	NO	NO	NO	NO	N	NO	-	YES	NO	YES	YES	NO	YES	YES	YES	YES	-	-	N
48	B/o R twin-1	NO	NO	NO	NO	N	NO	-	YES	NO	NO	NO	NO	NO	NO	YES	NO	-	-	N
49	B/o M	NO	NO	NO	NO	Y	YES	1	YES	YES	YES	NO	NO	YES	NO	YES	NO	44263	zone 2 stage 1	EARLY
50	B/o r twin-2	NO	NO	NO	NO	N	NO	-	YES	NO	NO	NO	NO	YES	NO	YES	NO	-	-	N
51	B/o Y twin-1	NO	NO	NO	YES	Y	YES	7	YES	YES	YES	YES	NO	YES	YES	YES	NO	-	-	N
52	B/o S twin-2	NO	NO	NO	NO	N	NO	-	YES	NO	NO	NO	NO	YES	NO	NO	NO	-	-	N
53	B/o Y twin-2	NO	NO	NO	YES	Y	YES	5	YES	YES	YES	YES	YES	YES	YES	YES	YES	44337	zone 2 satge 2	EARLY
54	B/o B	YES	NO	NO	NO	Y	YES	6	NO	NO	NO	YES	NO	YES	YES	NO	NO	44378	zone 2 stage 2 , mo prepluse disease	EARLY
55	B/o K	NO	NO	NO	NO	Y	YES	2	YES	NO	NO	YES	YES	YES	NO	YES	NO	-	-	N
56	B/o K	YES	NO	NO	YES	N	NO	-	YES	NO	NO	YES	NO	YES	YES	NO	NO	-	-	N

S.No.	Name	Sepsis	Feeding	EBM +HMF	EBM +HMF + MCT OIL	Date / current Gestation	Birth weight (gms)0	Current Weight (gms) 1	Birth weight group	percentage of gain/loss	Abdominal girth_Gain/ Loss	Date/ Abdominal Girth in cm	Increased	BPD yes/no	IVH yes/no	NICU Stay (days) Decreased	NICU Stay	Date / current Gestation	Current Weight 2	percentage %	gain/loss
1	B/O K	NO	1	YES	NO	02-03-2020	990	1335	1	10	gain	-	NO	yes	no	NO	35	30-07-2020	2460	11	gain
2	b/o M	YES	2	NO	YES	25-02-2020	1090	1190	2	3	gain	-	NO	No	no	NO	36	25-06-2020	2150	11	gain
3	B/o R	YES	2	NO	YES	22-01-2020	800	1310	1	7	gain	-	NO	yes	no	NO	77	17-07-2020	2700	15	gain
4	B/o T	YES	2	NO	YES	17-02-2020	940	1340	1	12	gain	-	NO	No	no	NO	34	30-06-2020	2750	16	gain
5	B/o J	NO	2	NO	YES	12-04-2020	1490	1465	2	1	loss	-	NO	No	no	NO	22	31-07-2020	2910	16	gain
6	B/o M twin 1	NO	2	NO	YES	06-06-2020	1200	2120	2	18	gain	29	YES	yes	no	NO	48	29-10-2020	3400	14	gain
7	B/o P	YES	2	NO	YES	22-05-2020	805	1620	1	12	gain	27	YES	yes	no	NO	60	27-11-2020	3300	19	gain
8	B/o S twin-1	NO	2	NO	YES	25-07-2020	1160	1540	2	22	gain	-	NO	No	no	NO	17	29-12-2020	2900	15	gain
9	B/o S twin-2	NO	2	NO	YES	19-08-2020	1060	1515	2	15	gain	-	NO	No	no	NO	31	27-12-2020	3400	20	gain
10	B/o R	NO	2	NO	YES	24-08-2020	1300	1590	2	16	gain	-	NO	No	no	NO	18	25-11-2020	3010	16	gain
11	B/o S	YES	2	NO	YES	26-08-2020	1200	1290	2	3	gain	-	NO	No	no	NO	26	01-01-2021	2715	16	gain
12	B/o A	NO	2	NO	YES	30-08-2020	1490	1700	2	16	gain	-	NO	No	no	NO	11	25-12-2020	3280	18	gain
13	B/o P twin-2	NO	2	NO	YES	28-08-2020	1280	2020	2	28	gain	-	NO	No	no	NO	26	05-01-2020	3925	21	gain
14	B/o S	NO	2	NO	YES	28-08-2020	980	1225	1	18	gain	-	NO	No	no	NO	14	13-12-2020	2300	12	gain
15	B/o S	YES	2	NO	YES	15-09-2020	1100	1400	2	16	gain	-	NO	No	no	NO	19	30-12-2020	2610	13	gain
16	B/o M	NO	2	NO	YES	12-09-2020	1330	1400	2	4	gain	-	NO	No	no	NO	20	30-12-2020	2410	11	gain
17	B/o H twin-2	NO	2	NO	YES	08-09-2020	1175	1580	2	14	gain	-	NO	No	no	NO	28	04-01-2021	3100	17	gain
18	B/o H twin-1	NO	2	NO	YES	08-09-2020	1200	1380	2	6	gain	-	NO	No	no	NO	30	25-12-2020	2980	18	gain
19	B/o J	NO	1	YES	NO	18-10-2020	1465	1410	2	4	loss	-	NO	No	no	NO	13	31-01-2021	2410	11	gain
20	B/o R	NO	1	YES	NO	16-10-2020	1060	1280	2	9	gain	-	NO	yes	no	NO	32	07-01-2021	1882	7	gain
21	b/o H	YES	2	NO	YES	19-10-2020	940	1400	1	12	gain	-	NO	yes	no	NO	40	02-02-2021	2250	9	gain
22	B/o K	NO	2	NO	YES	18-11-2020	1340	1700	2	13	gain	-	NO	No	no	NO	28	27-12-2020	2210	6	gain
23	B/o S	YES	1	YES	NO	06-11-2020	1020	1460	2	8	gain	25	YES	No	no	NO	52	15-03-2020	2000	6	gain
24	B/o S	YES	1	YES	NO	04-11-2020	865	1560	1	14	gain	23	YES	No	no	NO	45	27-03-2020	2100	6	gain
25	B/o R twin-1	YES	1	YES	NO	17-11-2020	885	1460	1	14	gain	-	NO	yes	no	NO	39	03-03-2021	1950	5	gain
26	B/o D	NO	1	YES	NO	19-11-2020	1370	1760	2	16	gain	-	NO	No	no	NO	24	15-03-2021	2310	6	gain
27	B/o S	YES	1	YES	NO	20-11-2020	840	1560	1	13	gain	-	NO	No	no	NO	53	27-03-2021	1810	3	gain
28	B/o R twin-2	YES	2	NO	YES	17-11-2020	780	1320	1	9	gain	-	NO	yes	no	NO	58	27-04-2021	2500	13	gain
29	B/o G	YES	1	YES	NO	08-12-2020	1420	1590	2	14	gain	-	NO	No	no	NO	12	27-03-2021	2810	14	gain
30	B/o N	YES	1	YES	NO	29-11-2020	1300	1800	2	11	gain	26	YES	No	no	NO	43	27-04-2021	2390	13	gain
31	B/o H	YES	1	YES	NO	25-12-2020	1040	1300	2	8	gain	-	NO	No	no	NO	22	15-04-2021	2600	15	gain
32	B/o S	YES	2	NO	YES	04-05-2020	980	1320	1	13	gain	24	YES	No	no	NO	27	27-09-2020	2620	14	gain
33	B/O G twin-1	NO	1	YES	NO	17-12-2020	1380	1760	2	10	gain	-	NO	No	no	NO	37	27-04-2021	2910	13	gain
34	B/o R twin-2	NO	1	YES	NO	10-11-2020	690	1760	1	18	gain	-	NO	yes	no	NO	57	27-04-2021	2770	11	gain
35	B/o R	YES	1	YES	NO	20-01-2021	1080	1420	2	17	gain	-	NO	No	no	NO	20	18-05-2021	2520	12	gain
36	B/o G	YES	2	NO	YES	17-12-2021	1220	1515	2	8	gain	-	NO	No	no	NO	38	28-04-2021	2830	15	gain
37	B/o A	YES	2	NO	YES	12-05-2020	1090	1360	2	8	gain	25	YES	No	no	NO	32	30-09-2020	2700	15	gain
38	B/o M	YES	2	NO	YES	11-06-2020	1480	1500	2	3	gain	-	NO	No	no	NO	6	15-08-2020	2500	11	gain
39	B/o U	YES	2	NO	YES	22-06-2020	1080	1740	2	14	gain	-	NO	No	no	NO	48	30-11-2020	3100	15	gain
40	B/O A	YES	1	YES	NO	18-12-2020	1030	1500	2	10	gain	-	NO	No	no	NO	40	23-05-2021	3100	18	gain
41	B/o M	YES	1	YES	NO	12-12-2020	830	1500	1	12	gain	-	NO	yes	no	NO	54	27-05-2021	3500	22	gain
42	B/o P	YES	1	YES	NO	22-12-2020	1000	1520	2	10	gain	-	NO	yes	no	NO	51	29-05-2021	3335	20	gain
43	B/o A	YES	2	NO	YES	15-07-2020	940	1480	1	13	gain	-	NO	No	no	NO	40	21-11-2020	3100	18	gain
44	B/o N	YES	2	NO	YES	20-02-2020	1420	1380	2	3	loss	-	NO	No	no	NO	16	31-05-2020	3020	18	gain
45	B/o R	YES	1	YES	NO	19-01-2021	1150	1740	2	11	gain	-	NO	yes	no	NO	53	17-06-2021	3220	17	gain
46	B/o G	NO	1	YES	NO	18-01-2021	1200	1680	2	14	gain	-	NO	No	no	NO	34	15-05-2021	2970	14	gain
47	b/o D	NO	1	YES	NO	17-02-2021	1160	1340	2	7	gain	25	YES	No	no	NO	20	27-06-2021	3000	18	gain
48	B/o R twin-1	NO	1	YES	NO	28-02-2021	1460	1700	2	14	gain	-	NO	No	no	NO	10	17-05-2021	2600	10	gain
49	B/o M	NO	1	YES	NO	31-01-2021	1230	1880	2	15	gain	-	NO	No	no	NO	38	21-06-2021	3300	16	gain
50	B/o r twin-2	NO	1	YES	NO	28-02-2021	1360	1420	2	4	gain	-	NO	No	no	NO	14	27-05-2021	2950	17	gain
51	B/o Y twin-1	NO	1	YES	NO	13-03-2021	1120	1920	2	13	gain	-	NO	yes	no	NO	60	23-08-2021	3520	18	gain
52	B/o S twin-2	NO	2	NO	YES	24-10-2020	1400	1920	2	17	gain	-	NO	No	no	NO	31	12-02-2021	3280	15	gain
53	B/o Y twin-2	YES	1	YES	NO	13-03-2021	1130	1920	2	13	gain	-	NO	yes	no	NO	59	25-07-2021	3370	16	gain
54	B/o B	YES	2	NO	YES	17-09-2021	1460	1520	2	3	gain	27	YES	No	no	NO	16	21-09-2021	2300	9	gain
55	B/o K	YES	2	NO	YES	02-05-2021	1080	1765	2	10	gain	26	YES	yes	yes	NO	66	15-10-2021	2905	13	gain
56	B/o K	NO	2	NO	YES	15-07-2020	1200	1420	2	9	gain	22	YES	No	no	NO	22	15-12-2020	3155	19	gain

S.No.	Name	MRD No	DOB	DOA	DOD	Duration of hospital stay(days)	Gender	Gestation (weeks)	Gestation (weeks) group	GROWTH STATUS	Mode of Delivary	Birth weight in Grams	APGAR Scores (for inborn) at 1min	APGAR Scores at 5 min	REASON FOR ADMISSION_Prematurity	Respiratory symptom	Respiratory failure	Sepsis evaluation	Peri natal Asphyxia	Seizures	Hypoglycemia	Hyper Bilirubinemia
57	B/o B	940534	06-07-2021	06-07-2021	20-07-2021	15	female	32	2	SGA	LSCS	1290	5	8	YES	YES	NO	NO	NO	NO	NO	NO
58	B/o P	1122243	14-06-2021	14-06-2021	22-07-2021	39	female	30	2	AGA	LSCS	950	5	7	YES	YES	YES	NO	YES	NO	NO	NO
59	B/o H	1116261	02-06-2021	02-06-2021	22-07-2021	50	male	29	1	AGA	LSCS	940	6	7	YES	YES	NO	NO	YES	NO	NO	NO
60	B/O K	921322	06-04-2020	06-04-2020	21-04-2020	15	male	32	2	SGA	LSCS	1300	4	7	YES	YES	YES	NO	YES	NO	NO	NO
61	B/o C	943414	15-07-2020	15-07-2020	04-09-2020	52	male	28	1	AGA	NVD	1175	7	8	YES	YES	NO	NO	NO	NO	NO	NO
62	B/o S	932601	07-06-2020	07-06-2020	30-06-2020	25	female	32	2	SGA	LSCS	1360	5	7	YES	YES	NO	NO	YES	NO	NO	NO
63	B/o K	927848	20-05-2020	20-05-2020	10-06-2020	22	male	30	2	AGA	LSCS	1450	8	9	YES	YES	NO	NO	NO	NO	NO	NO
64	B/0 H twin-2	925148	05-05-2020	05-05-2020	15-05-2020	11	male	33	2	SGA	NVD	1380	8	9	YES	YES	NO	NO	NO	NO	NO	NO
65	B/o A	920778	30-03-2020	30-03-2020	23-04-2020	25	female	31	2	SGA	LSCS	920	8	9	YES	YES	NO	NO	NO	NO	NO	NO
66	B/o K twin-1	1147033	02-08-2021	02-08-2021	06-09-2021	34	male	29	1	AGA	LSCS	1180	7	8	YES	YES	NO	NO	NO	NO	NO	NO
67	B/o K twin -2	1147037	02-08-2021	02-08-2021	06-09-2021	34	female	29	1	AGA	LSCS	1380	7	8	YES	YES	YES	NO	NO	NO	NO	NO
68	B/o A	1159027	22-08-2021	22-08-2021	13-09-2021	22	male	31	2	AGA	LSCS	1235	7	9	YES	YES	YES	NO	NO	NO	NO	NO
69	B/o S	1141762	23-07-2021	23-07-2021	03-09-2021	43	female	30	2	AGA	LSCS	1100	5	8	YES	YES	YES	NO	YES	NO	NO	NO
70	B/o S twin-2	1150004	07-08-2021	07-08-2021	03-09-2021	28	male	31	2	AGA	NVD	1280	5	8	YES	YES	YES	NO	NO	NO	NO	NO
71	B/o S twin-1	1149996	07-08-2021	07-08-2021	03-09-2021	28	male	31	2	AGA	NVD	1260	7	8	YES	YES	NO	NO	NO	NO	NO	NO
72	B/o B	1155027	15-08-2021	15-08-2021	23-09-2021	34	male	27	1	AGA	NVD	1040	7	8	YES	YES	NO	NO	NO	NO	NO	NO
73	B/o J	1163482	29-08-2021	29-08-2021	03-09-2021	16	male	32	2	AGA	LSCS	1340	8	9	YES	YES	NO	NO	NO	NO	NO	NO
74	B/o R	11333504	23-07-2021	23-07-2021	29-07-2021	6	male	34	2	AGA	LSCS	1380	-	-	YES	YES	NO	NO	NO	NO	NO	NO
75	B/o G	1138858	18-07-2021	18-07-2021	02-09-2021	47	male	30	2	SGA	LSCS	790	5	7	YES	YES	YES	NO	NO	NO	NO	NO
76	B/o s	1125085	20-06-2021	02-08-2021	09-07-2021	20	female	32	2	SGA	NVD	1140	-	-	YES	YES	NO	NO	NO	NO	NO	NO
77	B/o S twin -2	930293	30-05-2020	30-05-2020	24-06-2020	26	female	30	2	AGA	LSCS	1400	7	8	YES	YES	NO	NO	NO	NO	NO	NO
78	B/o M twin-1	1133508	07-07-2021	07-07-2021	05-08-2021	30	male	30	2	AGA	LSCS	1280	4	7	YES	YES	NO	NO	NO	NO	NO	NO
79	B/o M twin-2	1133509	07-07-2021	07-07-2021	05-08-2021	30	male	30	2	SGA	LSCS	980	3	7	YES	YES	YES	NO	NO	NO	NO	NO
80	B/o I	1110544	18-05-2021	18-05-2021	15-08-2021	90	female	26	1	AGA	LSCS	820	3	7	YES	YES	YES	NO	NO	NO	NO	NO
81	B/o S	1126976	20-06-2021	24-06-2021	13-07-2021	24	male	31	2	AGA	LSCS	1200	-	-	YES	YES	NO	YES	NO	NO	NO	NO
82	S	1153348	07-08-2021	12-08-2021	30-08-2021	23	female	31	2	AGA	NVD	1250	-	-	YES	YES	NO	NO	NO	NO	NO	NO
83	S	1141812	23-07-2021	23-07-2021	03-09-2021	43	male	28	1	AGA	LSCS	1020	7	8	YES	YES	YES	NO	NO	NO	NO	NO
84	J	1153358	07-08-2021	12-08-2021	30-08-2021	24	female	24	1	AGA	NVD	1490	-	-	YES	YES	YES	NO	NO	YES	NO	NO
85	B/o V	1106779	11-05-2021	11-05-2021	05-06-2021	26	male	30	2	AGA	LSCS	1080	7	9	YES	YES	NO	NO	NO	NO	NO	NO
86	B/O p	1156749	18-08-2021	18-08-2021	30-08-2021	13	female	34	2	SGA	LSCS	1470	8	10	YES	YES	YES	NO	NO	NO	NO	NO
87	B/o D twin -2	1172672	13-09-2021	13-09-2021	26-09-2021	14	female	32	2	AGA	NVD	1330	-	-	YES	YES	NO	NO	NO	NO	NO	NO
88	B/o S	1175763	18-09-2020	18-09-2020	09-11-2020	51	male	28	1	AGA	LSCS	1040	8	9	YES	YES	YES	NO	NO	NO	NO	NO
89	B/o J twin -1	1172772	13-09-2021	13-09-2021	09-11-2021	65	male	27	1	AGA	LSCS	1080	6	9	YES	YES	NO	NO	NO	NO	NO	NO
90	B/o R	1208894	16-11-2021	16-11-2021	04-12-2021	21	male	21	1	AGA	LSCS	1480	7	8	YES	YES	NO	NO	NO	NO	NO	NO

S.No.	Name	Metabolic evaluation	Small for gestational Age	Large for gestational age	Birth asphyxia requiring bag and mask evaluation	BPD	Need for ventilation	Duration of ventillatory support(days)	RDS	Need for surfactant	Apnea of pre maturity	Feed intolerance	Need for ionotropes	Need for CPAP	NEC	Need for phototherapy	Need for exchange transfusion	Abnormal ROP Screening	Findings	ROP
57	B/o B	NO	NO	NO	YES	N	NO	-	YES	NO	NO	NO	NO	YES	NO	YES	NO	-	-	N
58	B/o P	NO	NO	NO	YES	Y	YES	4	YES	YES	YES	YES	YES	YES	YES	YES	NO	-	-	N
59	B/o H	NO	NO	NO	YES	N	NO	-	YES	NO	NO	YES	NO	YES	YES	YES	NO	-	-	N
60	B/O K	NO	NO	NO	YES	Y	YES	11	YES	NO	YES	NO	YES	YES	NO	YES	NO	-	-	N
61	B/o C	NO	NO	NO	NO	N	NO	-	YES	NO	YES	NO	NO	YES	YES	YES	NO	-	-	N
62	B/o S	NO	YES	NO	YES	Y	YES	4	YES	YES	NO	NO	NO	YES	NO	YES	NO	-	-	N
63	B/o K	NO	NO	NO	NO	N	NO	-	YES	NO	NO	NO	NO	YES	NO	YES	NO	-	-	N
64	B/0 H twin-2	NO	YES	NO	NO	N	NO	-	YES	NO	NO	NO	NO	YES	NO	YES	NO	-	-	N
65	B/o A	NO	YES	NO	NO	Y	YES	4	YES	YES	YES	NO	NO	YES	YES	YES	NO	-	-	N
66	B/o K twin-1	NO	NO	NO	NO	N	NO	-	YES	NO	YES	YES	NO	YES	YES	YES	NO	-	-	N
67	B/o K twin -2	NO	NO	NO	NO	Y	YES	4	YES	YES	NO	NO	NO	YES	NO	YES	NO	-	-	N
68	B/o A	NO	NO	NO	YES	Y	YES	1	YES	YES	NO	NO	NO	YES	NO	YES	NO	-	-	N
69	B/o S	NO	NO	NO	YES	Y	YES	3	YES	YES	YES	YES	NO	YES	NO	YES	NO	-	-	N
70	B/o S twin-2	NO	NO	NO	YES	Y	YES	2	YES	YES	NO	YES	NO	YES	NO	YES	NO	-	-	N
71	B/o S twin-1	NO	NO	NO	NO	N	NO	-	YES	NO	YES	YES	NO	YES	YES	YES	NO	-	-	N
72	B/o B	NO	NO	NO	YES	Y	YES	4	YES	YES	NO	NO	NO	YES	NO	NO	NO	-	-	N
73	B/o J	NO	YES	NO	NO	N	NO	-	YES	NO	NO	NO	NO	YES	NO	YES	NO	-	-	N
74	B/o R	NO	NO	NO	NO	N	NO	-	YES	NO	YES	NO	NO	NO	NO	NO	NO	-	-	N
75	B/o G	NO	YES	NO	YES	Y	YES	3	YES	YES	YES	YES	NO	YES	YES	YES	NO	-	-	N
76	B/o s	NO	YES	NO	NO	N	NO	-	YES	NO	YES	NO	NO	YES	NO	YES	NO	-	-	N
77	B/o S twin -2	NO	NO	NO	NO	N	NO	-	YES	NO	NO	NO	NO	YES	NO	YES	NO	-	-	N
78	B/o M twin-1	NO	NO	NO	YES	N	NO	-	YES	YES	YES	YES	NO	YES	NO	YES	NO	-	-	N
79	B/o M twin-2	NO	YES	NO	YES	Y	YES	13	YES	YES	YES	YES	YES	YES	YES	YES	NO	-	-	N
80	B/o I	NO	NO	NO	YES	Y	YES	15	YES	YES	YES	YES	NO	YES	YES	YES	NO	-	-	N
81	B/o S	NO	NO	NO	NO	N	NO	-	YES	NO	NO	NO	NO	NO	YES	YES	NO	-	-	N
82	S	NO	NO	NO	NO	N	NO	-	YES	NO	YES	NO	NO	YES	NO	NO	NO	-	-	N
83	S	NO	NO	NO	YES	Y	YES	8	YES	YES	NO	NO	YES	YES	NO	YES	NO	-	-	N
84	J	NO	NO	NO	NO	N	YES	8	YES	YES	YES	NO	NO	NO	NO	YES	NO	-	-	N
85	B/o V	NO	NO	NO	YES	Y	YES	3	YES	YES	NO	NO	NO	YES	NO	NO	NO	-	-	N
86	B/O p	NO	YES	NO	YES	Y	YES	2	YES	YES	NO	NO	NO	YES	NO	YES	NO	-	-	N
87	B/o D twin -2	NO	NO	NO	NO	N	NO	-	YES	NO	NO	YES	NO	YES	NO	NO	NO	-	-	N
88	B/o S	NO	NO	NO	YES	Y	YES	1	YES	YES	YES	NO	NO	YES	YES	YES	NO	-	-	N
89	B/o J twin -1	NO	NO	NO	YES	Y	YES	4	YES	YES	YES	NO	NO	YES	NO	NO	NO	-	-	N
90	B/o R	NO	NO	NO	YES	N	NO	-	YES	NO	YES	NO	NO	YES	NO	YES	NO	-	-	N

S.No.	Name	Sepsis	Feeding	EBM +HMF	EBM +HMF + MCT OIL	Date / current Gestation	Birth weight (gms)0	Current Weight (gms) 1	Birth weight group	percentage of gain/loss	Abdominal girth_Gain/ Loss	Date/ Abdominal Girth in cm	Increased	BPD yes/no	IVH yes/no	NICU Stay (days) Decreased	NICU Stay	Date / current Gestation	Current Weight 2	percentage %	gain/loss
57	B/o B	NO	1	YES	NO	06-07-2020	1260	1440	2	12	gain	-	NO	No	no	NO	15	21-10-2020	3940	25	gain
58	B/o P	NO	1	YES	NO	14-06-2021	950	1300	1	9	gain	-	NO	No	no	NO	36	29-10-2021	2918	18	gain
59	B/o H	YES	1	YES	NO	02-06-2021	940	1440	1	10	gain	-	NO	No	no	NO	49	27-10-2021	2960	17	gain
60	B/O K	YES	1	YES	NO	06-04-2020	1300	1480	2	12	gain	-	NO	No	no	NO	15	11-08-2021	3100	18	gain
61	B/o C	NO	2	NO	YES	15-07-2020	1175	1680	2	10	gain	-	NO	yes	no	NO	50	28-12-2020	3380	19	gain
62	B/o S	YES	2	NO	YES	01-06-2020	1360	1300	2	1	loss	-	NO	No	no	NO	25	30-09-2020	2550	14	gain
63	B/o K	NO	1	YES	NO	20-05-2020	1450	1900	2	20	gain	-	NO	No	no	NO	20	30-08-2020	1900	19	gain
64	B/0 H twin-2	NO	1	YES	NO	05-05-2020	1380	1420	2	4	gain	-	NO	No	no	NO	11	23-08-2020	2700	14	gain
65	B/o A	NO	2	NO	YES	30-03-2020	920	1245	1	13	gain	-	NO	No	no	NO	25	29-07-2020	2275	11	gain
66	B/o K twin-1	NO	1	YES	NO	02-08-2021	1180	1375	2	8	gain	-	NO	No	no	NO	32	15-11-2021	2325	11	gain
67	B/o K twin -2	NO	1	YES	NO	02-08-2021	1380	1760	2	11	gain	-	NO	No	no	NO	32	15-11-2021	2700	10	gain
68	B/o A	NO	1	YES	NO	22-08-2021	1235	1300	2	3	gain	-	NO	No	no	NO	21	09-11-2021	2280	11	gain
69	B/o S	YES	1	YES	NO	23-07-2021	1100	1440	2	8	gain	-	NO	yes	no	NO	41	25-11-2021	2585	13	gain
70	B/o S twin-2	NO	1	YES	NO	07-08-2021	1280	1500	2	8	gain	-	NO	No	no	NO	25	25-11-2021	2730	14	gain
71	B/o S twin-1	NO	1	YES	NO	07-08-2021	1260	1440	2	6	gain	-	NO	No	no	NO	17	27-11-2021	2750	15	gain
72	B/o B	NO	2	NO	YES	15-08-2021	1040	1340	2	9	gain	-	NO	No	yes	NO	34	21-12-2021	2650	15	gain
73	B/o J	NO	1	YES	NO	29-08-2021	1340	1480	2	9	gain	-	NO	No	no	NO	16	21-12-2021	2500	11	gain
74	B/o R	NO	1	YES	NO	23-07-2021	1460	1600	2	23	gain	-	NO	No	no	NO	6	17-10-2021	2490	10	gain
75	B/o G	NO	1	YES	NO	18-07-2021	790	1000	1	4	gain	-	NO	yes	no	NO	47	16-12-2021	2330	15	gain
76	B/o s	YES	1	YES	NO	20-06-2021	1140	1340	2	10	gain	-	NO	No	yes	NO	16	02-09-2021	1560	2	gain
77	B/o S twin -2	NO	1	YES	NO	30-05-2020	1400	2200	2	31	gain	-	NO	No	no	NO	19	22-09-2021	3400	13	gain
78	B/o M twin-1	NO	1	YES	NO	07-07-2021	1280	14440	2	5	gain	-	NO	No	no	NO	28	27-11-2021	2840	15	gain
79	B/o M twin-2	YES	2	NO	YES	07-07-2021	980	1000	1	1	gain	24	YES	No	yes	NO	30	15-11-2021	2940	21	gain
80	B/o I	YES	2	NO	YES	18-05-2021	820	2120	1	14	gain	-	NO	yes	no	NO	90	27-11-2021	3730	18	gain
81	B/o S	YES	2	NO	YES	24-06-2021	1190	1300	2	5	gain	22	NO	No	yes	YES	22	21-11-2021	3010	19	gain
82	S	NO	2	NO	YES	12-08-2021	1180	1420	2	10	gain	-	NO	No	yes	NO	18	30-11-2021	3070	18	gain
83	S	YES	1	YES	NO	23-07-2021	1020	1560	2	13	gain	-	NO	yes	no	NO	40	23-12-2021	2920	15	gain
84	J	NO	2	NO	YES	12-08-2021	1355	1500	2	6	gain	-	NO	No	yes	NO	22	02-12-2021	2705	13	gain
85	B/o V	NO	2	NO	YES	01-05-2021	1080	1420	2	13	gain	-	NO	No	no	NO	24	21-09-2021	2480	12	gain
86	B/O p	NO	1	YES	NO	18-08-2021	1470	1420	2	3	loss	-	NO	yes	no	NO	10	23-11-2021	2480	12	gain
87	B/o D twin -2	NO	2	NO	YES	13-09-2021	1330	1240	2	9	loss	-	NO	No	yes	NO	10	27-12-2021	2500	14	gain
88	B/o S	NO	2	NO	YES	18-09-2020	1040	1460	2	8	gain	-	NO	No	no	NO	49	15-01-2020	2730	14	gain
89	B/o J twin -1	YES	2	NO	YES	13-09-2021	1080	1700	2	7	gain	-	NO	No	no	NO	10	19-11-2020	2985	14	gain
90	B/o R	NO	2	NO	YES	16-11-2021	1480	1760	2	13	gain	-	NO	No	no	NO	14	27-02-2021	3300	17	gain

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Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 22.01.2021 has approved the plan of thesis of **Dr. Navotam,** a student of your college for **MD Paediatrics** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis

Human milk fortifier and medium chain triglyceride oil for weight gain in very low birth weight neonates: a randomized controlled trial

Supervisor
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Dept. of Paediatrics,
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Co-Supervisor
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The student has to submit the three copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. ***If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.***
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

HUMAN MILK FORTIFIER AND MEDIUM CHAIN TRIGLYCERIDE OIL FOR WEIGHT GAIN IN VERY LOW BIRTH WEIGHT NEONATES: A RANDOMIZED CONTROLLED TRIAL

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

PAEDIATRICS

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

NOVEMBER, 2019

DR. NAVOTAM

DEPARTMENT OF PAEDIATRICS
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

TITLE	Human milk fortifier and medium chain triglyceride oil for weight gain in very low birth weight neonates: A randomized controlled trial
DEGREE	MD Paediatrics
NAME OF THE CANDIDATE	Dr. Navotam
SUPERVISOR	Dr. Kamaldeep Arora, Associate Professor, Department of Pediatrics, DMC&H, Ludhiana
CO – SUPERVISOR	Dr. Gurdeep Singh Dhooria, Associate Professor Department of Pediatrics, DMC&H, Ludhiana
INSTITUTION	Dayanand Medical College & Hospital, Ludhiana
UNIVERSITY	Baba Farid University of Health Sciences, Faridkot

INTRODUCTION: Infants born prematurely have increased nutrient needs compared to those born at term. Provision of unfortified human milk has subsequently been linked to sub optimal growth (development of EUGR), reduced bone density, long term outcome like ROP/ Neurodevelopmental delay. The use of commercial human milk fortifiers allows for a more optimal provision of essential nutrients to meet premature infant requirements. MCT oil when supplemented to premature neonates who were given 3 gm/ kg/ day gained body weight better than control group. But still the strategy is not clear that whether adding MCT along with HMF would help in weight gain and hence in long term outcome like neurodevelopment, and ROP/BPD. This study is in the direction to reveal the effect of HMF along with MCT oil on growth & development of infant.

AIM OF STUDY: 1) To compare the weight gain in HMF & MCT Oil adding to breast milk as compared to adding only HMF to breast milk in VLBW infants.

2) To compare the duration of stay in hospital.

3) Incidences of BPD and ROP on use of HMF and MCT oil.

MATERIALS & METHODS: Randomized controlled Trial, Non blinded.

CLINICAL SIGNIFICANCE: Despite the favorable results regarding the use of HMF, further studies are needed to improve and individualize the nutrition of very low birth weight preterm infants, taking into consideration the composition of maternal milk and each new-born's needs. It is possible that new studies might demonstrate results obtained with the use of fortifiers extracted from human milk.

1. Nutritional Needs of VLBW Infants
   - 110-130 kcals/kg
   - 3.4-4.3 grams protein/kg
   - 100-220 mg calcium/kg
   - 60-140 mg phosphorus/kg

KEYWORDS - HMF, MCT, EUGR (Extra-uterine growth retardation).

(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"HUMAN MILK FORTIFIER AND MEDIUM CHAIN TRIGLYCERIDE OIL FOR WEIGHT GAIN IN VERY LOW BIRTH WEIGHT NEONATES: A RANDOMIZED CONTROLLED TRIAL"** exist in the Department of Paediatrics, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

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APPROVAL PROFORMA
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Likely date of appearing in PG examination	May 2022
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PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

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5	TITLE OF THE TOPIC	HUMAN MILK FORTIFIER AND MEDIUM CHAIN TRIGLYCERIDE OIL FOR WEIGHT GAIN IN VERY LOW BIRTH WEIGHT NEONATES: A RANDOMIZED CONTROLLED TRIAL

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Globally, about 18 million infants are born with a birth weight of <2500g every year.[1] Though these low birth weight (LBW) infants constitute only about 14% of the total live births, they account for 60-80% of total neonatal deaths.[2] Most of these deaths can be prevented with extra attention to warmth, prevention of infections and more importantly, optimal feeding. Optimal feeding of low birth weight (LBW) infants improves their immediate survival and subsequent growth & development. Being a heterogeneous group comprising term and preterm neonates, their feeding abilities, fluid and nutritional requirements are quite different from normal birth weight neonates.

Provision of adequate nutrition is central to effective care of ELBW and VLBW infants. They are born with limited nutrient reserves, immature pathways for nutrient absorption and metabolism, and higher nutrient demands. Moreover medical conditions associated with extreme prematurity both alter requirements for and complicate the adequate delivery of nutrients.

Poor weight gain and postnatal growth of preterm neonates continues to be a major problem. Intrauterine growth retardation is an additional risk factor in the growth of preterm neonates. Breast milk is considered as the best food for the neonates due to its several nutritional and immunologic advantages but this has been well established that human milk is an inadequate source of protein and minerals and calories for growing premature babies.[3] Since intrauterine accretion of nutrients occurs mainly in the later part of the third trimester, VLBW neonates (usually born before 32 weeks gestation) have low body stores at birth. Hence, they require supplementation of various nutrients.[4] Infants who are usually born before 32-34 weeks gestation have inadequate body stores of most of the nutrients. Expressed breast milk has inadequate amounts of protein, energy, calcium, phosphorus, trace elements (iron, zinc) and vitamins (D, E and K) that are unable to meet their daily recommended intakes. Hence, these infants need multi-nutrient

supplementation till they reach term gestation (40 weeks postmenstrual age).[5] Nutritional management influences immediate survival as well as subsequent growth and development of VLBW neonates.

Extra uterine growth restriction (EUGR) is a major clinical problem in VLBW infants.[6] Growth failure in VLBW neonates results from the complex interaction of many factors, including morbidities affecting nutrient requirements, central nervous system damage, difficulties in suck and swallow coordination[7]; however, inadequate nutrition—especially during the first weeks of life—is considered largely responsible for this state.[8] Many studies have demonstrated that inadequate early nutrition exerts an adverse influence on long-term developmental outcome. Early nutrition could also influence the long term neurodevelopmental outcomes; malnutrition at a vulnerable period of brain development has been shown to have deleterious effects. Malnutrition is related to a decreased number of brain cells as well as deficits in behavior, learning, and memory.[9]

Very low birth weight babies need higher calories, protein and minerals to achieve adequate catch up growth.[10] The goal of nutritional management of ELBW and VLBW neonates are preservation of endogenous body stores, achievement of postnatal growth similar to intrauterine weight accretion and body composition, and maintenance of normal physiologic and metabolic process concomitant with minimizing complication and side effects. But are unable to meet these goals despite the use of parenteral nutrition and caloric supplementation of enteral feedings resulting in significant growth failure.

On basis of available literature exclusive breast feeding with HMF fortification or exclusive breast feeding with individual supplementation of MCT oil, vitamins and minerals show positive effect on growth. For HMF fortification frequent expression of milk is required prior to the feed with SF, whereas expression of breast milk is not needed in individual supplementation. Good hygiene is required in HMF while it is not required in individual supplementation. Fortification can result in

increase in milk osmolality[11], which may be associated with adverse effects such as feed intolerance and necrotizing enterocolitis.[12]

In present study we study the weight gain pattern in very low birth weight babies with EBM fortified with HMF and MCT oil.

6.2 REVIEW OF LITERATURE

Globally about 18 million neoantes are born with a birth weight of <2500 g every Year. Though these low birth weight (LBW) infants constitute only about 14%

Of the total live birth, they account for 60-80% of total neonatal deaths. Most of these deaths can be prevented with extra attention to warmth, prevention of infections and more importantly, optimal feeding. Optimal feeding of low birth weight (LBW) infants improves their immediate survival and subsequent growth and development. Being a heterogenous group comprising term and preterm neonates, their feeding abilities, fluid and nutritional requirements are quite different from normal birth weight infants.

Study done by Martins EC et al (2009) compared the weight and height gain and the frequency of clinical complications in preterm new borns weighing less than 1,500 g, exclusively fed human milk or fortified human milk until reaching 1,800 g.15 Prospective double blind randomized controlled trial involving 40 preterm infants weighing <1,500 g at birth and ≤34 weeks of gestational age. Daily weight gain, weekly length and head circumference gain, nutritional variables and clinical complications were compared. Human milk fortification resulted in better growth, the weight gain was 24.4 and 21.1 g/day ($p = 0.075$). There were no significant clinical complications.[13]

Study done by Mukhopadhyay K et al studied the effects of human milk fortification on 166 infants (Preterm infants weighing ≤1500 grams and ≤34 weeks of gestation) on short term growth and biochemical parameters in preterm very low birth weight (VLBW) appropriate for gestation (AGA) and small for gestation (SGA) babies.16 Primary outcome measures were Short-term growth (daily weight, length and head circumference (HC) weekly) till discharge or 2 Kg. Fortification resulted in better growth in preterm VLBW babies as compared to control group.[14]

Study done by kuschel CA, Harding IE (1998) that Fortification of expressed breast milk with HMF increases the nutrient content of the milk with out compromising its other beneficial effects (such as

reduction of NEC, infections, etc.). Experimental studies have shown that the use of fortified human milk results in net nutrient retention that approaches or is greater than expcted intrauterine rates of accretion in preterm infants. Though there are concerns about the increase in osmolality, clinical studies have not shown any significant adverse effects following fortification of human milk. The Cochrane review on fortification found short term improvement in weight gain, linear and head growth with out any increase in adverse effects such as NEC.[15]

Study done by Beijing Da Xue Xue Bao Yi Xue Ban (2016) indicates that use HMF for premature infants may ensure the same growth pattern as those fed by premature formula, promote the calcium absorption, decrease the incidence of sepsis and feeding intolerance, and does not increase the incidence of necrotizing enterocolitis.[16]

Use of a LHMF in an unrestricted NICU population resulted in an increase in clinical complications within a high-acuity NICU, including metabolic acidosis and poor growth. Although further research is needed to assess outcomes among infants with a variety of clinical acuities, gestational ages, and weights to confirm these findings, based on this experience, caution is urged to avoid potential risks.[17]

Study done by Colaizy TT, Carlson S, Saftlas AF, Morriss FH JBMC Pediatr. 2012; that 97% of infants received human milk, 51% received > 75% of all enteral intake as human milk.

Those fed >75% human milk had a greater negative change in weight z-score from birth to discharge compared to infants receiving < 75% (-0.6 vs, -0.4, p = 0.03).

In infants receiving > 75% human milk, there was no significant difference in change in weight z-score by milk type (mother's own vs. donor)

Our current standardized fortification of human milk may not adequately support early postnatal growth.[18]

Study done by Moya F, Sisk PM, Walsh KR, Berseth CL,2012 Oct; preterm infants with BW <1250 grams randomized to get LHMF vs powder HMF (20% higher protein in LHMF).

At 28 days, the LHMF had a significantly higher achieved weight, length, head circumference, and linear growth rate than the control HMF (P = .004, P = .003, P = .04, and P = .01, control HMF (P .004, P .003, P .04, and P .01 respectively).[19]

Study done by Book LS, Herbst J J, Atherton SO, Jung AL, Pediatr 1975, shows that Osmolality is a critical determinant of feed tolerance (5-6). Milk fortification results in significant increase in osmolality (5,6). Feed intolerance may result in the reduction in nutrient intake which can explain lower weight gain compared to formula in VLBW infants. An association between hyper-osmolar feeds (³400 mOsm/ kg) and necrotizing enterocolitis has also been reported.[20]

The mean body weight gain was 19.7k 9.9 g/day in the infants given MCT oil and 17.9k12.5 g/day in the control group. The difference is not statistically significant. Energy intakes were 110.4 k 14.3 kcal/kg/day in the MCT group and 1 1 1.1 * 17.3 kcal/kg/day in the control group, while water intake was 137.6k6.9 ml/kg/day and 158.3k18.9 ml/kg/day respectively. Infants who were given MCT oil received almost the same energy intake, whereas the water intake was less than in the control group. The body weight gain of infants receiving MCT oil supplementation was better than in the control group in almost all daily energy intake categories, suggesting that MCT oil was utilized more efficiently than milk as an energy source.[21]

Study done by Verma GK et al. Int J Contemp Pediatr. 2018, Verma GK et al. study, on analysis of data, found that the weight gain of new borns who received HMF fortified maternal milk was 14.91 g/kg/day and overall fortified human milk has tremendous benefits in improving the growth and short term outcomes for the premature infant. Mother's own milk has clear advantages due to its composition. Premature infants need fortification of human milk to achieve growth as recommended. Based on the results of this study, we concluded that the supplementation with HMF, can result in a significant increase in growth (weight, linear and head growth).[5]

Daily body weight gains of infants substituted MCT oil were statistically better than the control group in energy intake 70s to 120s Kcal/kg/day

categories with the exception of 90s Kcal/kg/day category. To increase one gram of body weight, 5.2 kcal/kg/day and 5.8 kcal/ kg/day in MCT group and control group were needed respectively. Moreover if it is hypothesized that MCT oil is not used as energy, only 4.5 kcal/kg/day in the MCT group are necessary to increase one gram of body weight. All these data clearly suggest that MCT oil is definitely utilized for the weight gain of very pre- mature infants.[21]

We studied the efficacy of medium chain triglyceride (MCT) as an energy source in prema- ture infants. Infants who were given 3 g/kg/day of MCT oil gained body weight better than the control group in spite of a smaller water intake. This is advantageous to premature infants who need water restriction due to patent ductus arteriosus (PDA), bronchopulmo- nary dysplasia (BPD), etc. We also proved that MCT oil is rapidly absorbed and digested, by means of the '3C-trioctanoin breath test.[21]

After receiving milk-based formula for one week, 16 preterm infants, weighing 1,300 to 1,800 gm, were fed two isocaloric formulas containing either medium-chain or long-chain triglycerides for 15 days; the alternate formula was given for a second period of identical duration. While receiving MCT, the infants had greater (P smaller than 0.01) percent fat absorption (83.4 leads to 97.1%) and weight gain (7.5 leads to 11.5 gm/kg/100 calories). Because metabolic acidosis occurred with the LCT formula, the chloride content was adjusted to that of the MCT were confirmed and, in addition, there was a higher (P smaller than .01) percent retention of nitrogen (67.3 leads to 82.1).[22]

Okamoto E, Muttart CR, Zucker CL, Heird WC demonstrated failure of the resulting small increase in fat absorption incident to MCTs either to promote enhanced growth or to confer obvious clinical benefit does not support the increasing use of MCT formulas for routine feeding of LBW infants.[23]

Alice L. Bashinsky Concluded that for, the development and progression of ROP on of the important factors are extremely low birth weight and gestational age 30 weeks and under. There is need of preventing ROP which is along with prematurity through optimal

prenatal care. Reducing subsequent post-natal risk factors depends on optimal perinatal and postnatal care, as well as adhering to strict ROP screening guidelines. Recognizing and treating ROP in a timely fashion is critical for achieving the best visual outcome.[24]

6.3 AIMS AND OBJECTIVES OF THE STUDY

1. To Compare the weight gain with addition of HMF and MCT oil to breast milk as compared to adding HMF in very low birth weight babies.
2. To study the outcome with and without use of MCT oil.

7. MATERIALS AND METHODS

The study is designed as a randomized controlled trial for a period of one year from Jan 1st 2020 to March 31st 2021 (Including Followup) to be conducted at a level three neonatal intensive care unit of Dayanand medical college and hospital, Ludhiana.

Blinding: non blinding

7.1 Source of Data

Very Low birth weight babies admitted either as inborn or outborn in neonatal intensive care unit, who are on 100 ml/kg/day of expressed breast milk(EBM) receiving both human milk fortifier and MCT OIL.

7.2 METHOD OF COLLECTION OF DATA

Guardian/ Parents of patient fulfilling inclusion and exclusion criteria will be enrolled in the study. They will be informed about the purpose and nature of study, risk and benefits associated with participation in the study.

Daily weight monitoring will be done of Very low birth weight neonates receiving enteral nutrition along with HMF and MCT oil and evaluated accordingly till the time of discharge from NICU. Babies abdominal circumference will be monitored before giving every feeds.

Any abdominal circumference showing increase of more than 2 cm will be taken as significant.

To look for weight gain, the new born will be followed for 3 months post expected age of delivery.

We will randomly allocate the patients into 2 groups by a Random generation sequence. These sequence will be generated by an independent statistician who will be blinded to the study groups. 45 patients would be taken in each group, written consent will be taken from the parents/local guardians, and we follow them up till discharge and again 3 months later.

To compensate for attrition weight 45 patients would be taken in each group.

Randomization: Computer generated random number sequences will be generated, not otherwise involved in this study.

INCLUSION CRITERIA

1) All the VLBW neonates (<1500 gms) irrespective of the gestational age admitted at neonatal intensive care unit.

2. Both inborn and outborn babies to be included in the study.

EXCLUSION CRITERIA

1. Surgical conditions
2. Syndromic Babies
3. Parents/Guardian not giving consent

STUDY TYPE: Randomised Control Trial: Non Blinded.

DURATION OF STUDY: From then date of enrollment to one year and 3 months from Jan 1st 2020 to March 31st 2021 (Including Followup). We will follow them till 36 weeks or till discharge, which ever is later

OUTCOME: We closely monitor per day weight gain and look for the effect of HMF and HMF + MCT OIL comparatively on the both groups which have been included in the study and duration of stay in the hospital.

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups will be done using Student t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. For comparing categorical data, Chi square ($\chi 2$) test will be performed and exact test was used when the expected frequency is less than 5. A probability value (p value) less than 0.05 will be considered statistically significant. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith

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PROFORMA

S.No.

Name:

Father's name: MRD No:

DOB:

DOA: DOD:

Duration of hospital stay:

Gender: Male/Female

Gestation (weeks):

GROWTH STATUS: SGA/AGA/LGA

Address:

Mode of Delivary: NVD/FORCEPS/LSCS

Birth weight in Grams:

APGAR Scores (for inborn):

Signature of Candidates **Signature of Supervisor**

REASON FOR ADMISSION:

- Prematurity
- Respiratory symptom
- Respiratory failure
- Sepsis evaluation
- Peri natal Asphyxia
- Seizures
- Hypoglycemia
- Hyper Bilirubinemia
- Metabolic evaluation
- Small for gestational Age
- Large for gestational age

NEONATAL MORBIDITIES

- Birth asphyxia requiring bag and mask evaluation
- Need for ventilation
- Duration of ventillatory support
- RDS
- Need for surfactant
- Apnea of pre maturity
- Feed intolerance
- Need for ionotropes
- Need for CPAP :
- NEC

Signature of Candidates **Signature of Supervisor**

- Need for phototherapy
- Need for exchange transfusion
- Abnormal ROP Screening

Date	Findings

- Sepsis

OTHER INFORMATION

- Birth weight — Gestational Wt.

LMP – Gestation — NBS – Gestation

Feeding – EBM +HMF — EBM +HMF + MCT OIL

Signature of Candidates **Signature of Supervisor**

Daily weight Gain:

Date / current Gestation	Feeds	Birth Weight/Previous Weight	Current Weight	Gain/ Loss

Abdominal girth :

Date/Abdominal Girth in cm	Increased	Decreased

NICU Stay:

Signature of Candidates **Signature of Supervisor**

Followup

Date / current Gestation	Feeds	Birth Weight/Previous Weight	Current Weight	Gain/ Loss

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o..... am willing to participate in the study **"HUMAN MILK FORTIFIER AND MEDIUM CHAIN TRIGLYCERIDE OIL FOR WEIGHT GAIN IN VERY LOW BIRTH WEIGHT NEONATES: A RANDOMIZED CONTROLLED TRIAL"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

....

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **"HUMAN MILK FORTIFIER AND MEDIUM CHAIN TRIGLYCERIDE OIL FOR WEIGHT GAIN IN VERY LOW BIRTH WEIGHT NEONATES: A RANDOMIZED CONTROLLED TRIAL"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"HUMAN MILK FORTIFIER AND MEDIUM CHAIN TRIGLYCERIDE OIL FOR WEIGHT GAIN IN VERY LOW BIRTH WEIGHT NEONATES: A RANDOMIZED CONTROLLED TRIAL" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ